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# BULLETIN
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# *Kinetics of the Reduction of Selenious Acid by Sulfur Dioxide. I. Reduction in Acidic Solution with Hydrochloric Acid**

By Keinosuke HAMADA

(Received February 17, 1960)

Raw materials for the production of selenium depend heavily on a sludge and a copper slime, which are obtained as a by-product of a sulfuric acid factory and a copper refinery, respectively. In order to investigate the behavior of selenium at the sulfuric acid production plant, to increase the yield of selenium recoverable from the sulfuric acid plant source and to establish a simple method for the refining of these raw materials, the following series of studies were undertaken.

Consideration will be given first to the kinetics of the reduction of selenious acid in hydrochloric acid by sulfur dioxide. The percentage completion of these reactions is calculated by weighing the selenium precipitated from a solution. Sulfur dioxide is passed into a solution continuously, so that the reaction is of zero order with respect to sulfur dioxide.

It has been proved that the reduction of selenious acid was of the second order with respect to selenious acid. Furthermore, a general equation was derived for the rate constant of the reaction by studying the effects of hydrogen ion concentration and temperature upon it.

## Experimental

**Materials.**—1.752, 0.736, 0.368 and 0.172 mol./l. aqueous solution of selenious acid were prepared by dissolving extra pure reagent selenious acid in distilled water. On the other hand, 12, 6, 4.5 and 3% (by volume) hydrochloric acid solutions were prepared by diluting the first grade reagent hydrochloric acid (s. g. 1.18~1.19) with distilled water. The pH*1 values of these acid solutions were 0.02, 0.31, 0.42 and 0.59, which corresponded to 0.96, 0.49, 0.38 and 0.26 g. ion/l. of hydrogen ion concentration*2, respectively. Liquid sulfur dioxide was purchased from Befu Chemical Industrial Co.

**Measurements.**—Experimental solutions were prepared as follows. Ten milliliters of the above aqueous solutions of selenious acid were placed in a 200 ml. measuring flask, which was filled with the above-mentioned dilute hydrochloric acid. The solution was poured into a 300 ml. Erlenmeyer's flask, and kept at a constant temperature within ±0.1°C by a thermostat, and then sulfur dioxide was passed into the solution. The sulfur dioxide was initially passed through a washing bottle filled with water kept at the same constant temperature. Each of the selenious acid solutions was reduced by sulfur dioxide in four kinds of hydrochloric acid solutions at various temperatures.

After a certain period, the contents in an Erlenmeyer's flask was poured into 600 ml. of distilled water. In this way the reaction could be prevented owing to the decrease of the hydrogen ion concentration as well as temperature[1]. Precipitated selenium was filtered with a previously weighed glass filter (1G-4), washed by water, dried at 105~110°C in an air bath and then weighed.

Percentage completion of reaction is expressed with (precipitated selenium/initial selenium in the solution) × 100.

## Results and Discussion

**Selenious Acid Concentration Dependence of the Reduction of Selenious Acid.**—Concentrations of the prepared selenious acid solutions in hydrochloric acid were 0.0876, 0.0368, 0.0184 and 0.0086 mol./l., respectively. At constant temperature (70°C) and constant hydrogen ion concentration (0.49 g. ion/l.), these selenious acid solutions were reduced by sulfur dioxide. The weight of precipitated selenium was converted into percentage completion according to the above expression. Fig. 1 shows the selenious acid concentration dependence of the reduction of selenious acid by plotting the percentage completion against the elapsed time.

The values of half time ($t_{1/2}$) can be obtained from Fig. 1, and these are 100, 260, 460 and 1200 sec., respectively. When $a$ is the initial concentration of selenious acid (mol./l.), $p$ the quantity of reduced selenious acid (equal to precipitated selenium) after time $t$ (in sec.), $k_1$*3 the rate constant (l. mol$^{-1}$ sec$^{-1}$), $t_{1/2}$ the half time (sec.), and the reaction is of the $n$th order with respect to selenious acid, this reaction can be expressed mathematically by

$$-\mathrm{d}(a-p)/\mathrm{d}t = \mathrm{d}p/\mathrm{d}t = k_1(a-p)^n \qquad (1)$$

The solution of Eq. 1 is as follows,

* Presented at the 13th Annual Meeting of the Chemical Society of Japan, Tokyo, April, 1960.

*1 Measured by a pH-meter with 0.01 pH accuracy.

*2 Calculated from pH value.

1) J. W. Mellor: "A Comprehensive Treatise on Inorg. and Theoret. Chem." Vol. X, S, Se, p. 699.

*3 $k_1$ does not mean the rate constant of first order reaction, but the rate constant of the reduction of selenious acid in hydrochloric acid.

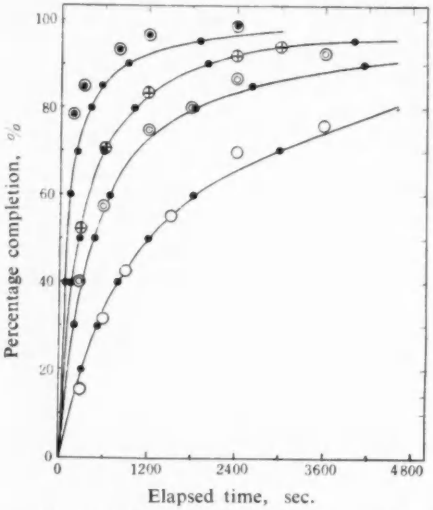


Fig. 1. $H_2SeO_3$ concn. dependence of the reduction of $H_2SeO_3$ in HCl at const. $[H^+]$ (0.49 g. ion/l.) and const. temp. (70°C).

- ◉ 0.0876 mol./l.
- ⊕ 0.0368 〃
- ◎ 0.0184 〃
- ○ 0.0086 〃
- • Calculated by Eq. 2, with $n$ equal to 2.

$$t=\{a^{n-1}-(a-p)^{n-1}\}/\{k_1(n-1)\times(a-p)^{n-1}a^{n-1}\} \quad (2)$$

If $t$ is equal to $t_{1/2}$, $p$ is equal to $a/2$. Making these substitutions for $t$ and $p$ in Eq. 2, the result is

$$t_{1/2}=(2^{n-1}-1)/\{k_1(n-1)a^{n-1}\} \quad (3)$$

When the values of the initial concentration of selenious acid and the experimentally determined half time ($t_{1/2}$) are substituted for $a$ and $t_{1/2}$ in Eq. 3, four equations are obtained;

$$1200=(2^{n-1}-1)/\{k_1(n-1)\times 0.0086^{n-1}\} \quad \text{(i)}$$

$$460=(2^{n-1}-1)/\{k_1(n-1)\times 0.0184^{n-1}\} \quad \text{(ii)}$$

$$260=(2^{n-1}-1)/\{k_1(n-1)\times 0.0368^{n-1}\} \quad \text{(iii)}$$

$$100=(2^{n-1}-1)/\{k_1(n-1)\times 0.0876^{n-1}\} \quad \text{(iv)}$$

Combining these equations, one can obtain the values of $n$ which are 2.27, 1.82, 2.10, 2.05, 2.07 and 1.98. The mean value of $n$ is 2.05, and from this it can be established that this reaction is one of second order with respect to selenious acid. As $n$ is equal to 2, the values of $k_1$ can be calculated from the above four equations.

**Temperature Dependence of the Reduction of Selenious Acid.**—At constant initial concentration of selenious acid (0.0184 mol./l.) and constant hydrogen ion concentration (0.49 g. ion/l.), selenious acid in hydrochloric acid is reduced by sulfur dioxide, when the temperature is at 70, 60, 55 and 50°C. Fig. 2 shows the plot of the percentage completion against the elapsed time based upon the experimental data. As $n$ is equal to 2, and the values of the initial concentration of selenious acid are known and the values of half time can be obtained from Fig. 2, upon making these substitutions for the values for $n$, $a$ and $t_{1/2}$ in Eq. 3, the rate constants at 70, 60, 55 and 50°C are 0.118, 0.042, 0.020 and 0.012 l. $mol^{-1}$ $sec^{-1}$, respectively.

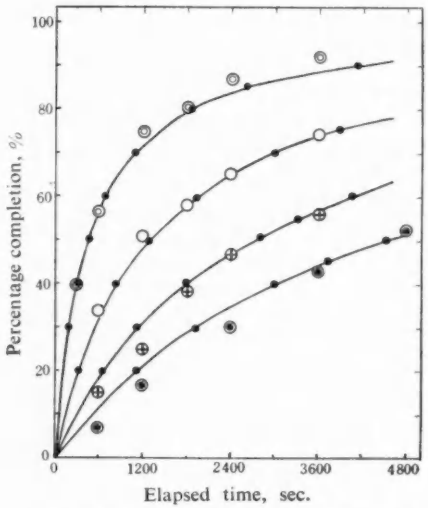


Fig. 2. Temperature dependence of the reduction of $H_2SeO_3$ at const. $[H_2SeO_3]$ (0.0184 mol./l.) and const. $[H^+]$ (0.49 g. ion/l.).

- ◎ 70°C
- ○ 60°C
- ⊕ 55°C
- ◉ 50°C
- • Calculated by Eq. 2, with $n$ equal to 2.

The influence of temperature on reaction velocity can be derived by plotting the logarithm of the rate constant, $\log k_1$, against the reciprocal of the absolute temperature, $1/T$ (Fig. 3). As Fig. 3 shows that the experimental points fall on a straight line, the energy of activation $E$ can be calculated from the value of the slope in Fig. 3.

The slope is equal to $-E/2.303R$[2]. The slope of the straight line in Fig. 3 is equal to $-5.35\times10^3$, and as $R$ is taken as 1.987 cal. $deg^{-1}$ $mol^{-1}$, it follows that for the reduction of selenious acid $E$ is 24.5 kcal./mol. Moreover,

2) S. Glasstone, "Elements of Physical Chemistry", Maruzen, Tokyo (1958), p. 607.

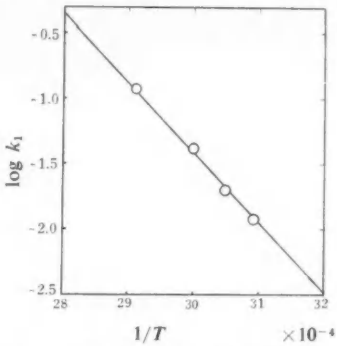


Fig. 3. Arrhenius' plot of the reduction of $H_2SeO_3$ by $SO_2$.

the rate constant $k_1$ is proportional to exp $(-E/RT)$.

**Hydrogen Ion Concentration Dependence of the Reduction of Selenious Acid.**—At a constant initial concentration of selenious acid (0.0184 mol./l.), the constant temperature (60°C) and various hydrogen ion concentrations (0.26, 0.38, 0.49 and 0.96 g. ion/l.), the selenious acid in hydrochloric acid were reduced by sulfur dioxide. These results are shown in Fig. 4.

Rate constant $k_1$ can be obtained from Eq. 3. Plotting the rate constant against the square of hydrogen ion concentration, it is seen in Fig. 5 that the experimental points fall on a straight line.

It is evident from Fig. 5 that rate constant $k_1$ is proportional to $[H^+]^2$.

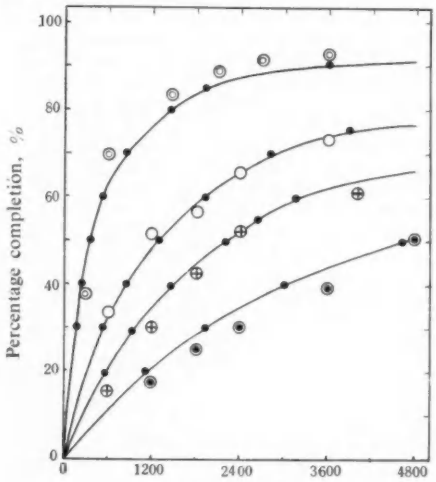


Fig. 4. $[H^+]$ dependence of the reduction of $H_2SeO_3$ at const. $[H_2SeO_3]$ (0.0184 mol./l.) and const. temp. (60°C).
- ◎ 0.96 g. ion/l.
- ○ 0.49 〃
- ⊕ 0.38 〃
- ◉ 0.26 〃
- • Calculated by Eq. 2, with $n$ equal to 2.

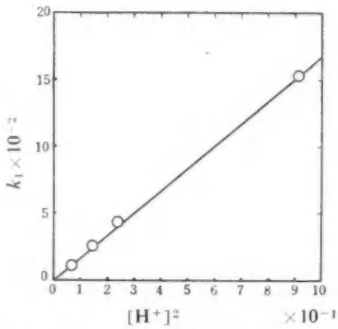


Fig. 5. Plot of $k_1$ against $[H^+]^2$.

When the temperature is equal to 60°C, hydrogen ion concentration is equal to 0.49 g. ion/l. and the initial concentration of selenious acid is equal to 0.0184 mol./l., the rate constant $k_1$ is evaluated to be 0.042 l. $mol^{-1}$ $sec^{-1}$. When these values*4 are adopted, the general Eq. 4 for rate constant can be derived, according to the above-mentioned temperature and hydrogen ion concentration dependence, that is,

$$k_1 = 2.054 \times 10^{15} \times [H^+]^2 \exp(-E/RT) \quad (4)$$

where $E$ is the energy of activation (24.5 kcal./mol.), $R$ the gas constant (1.987 cal. $deg^{-1}$ $mol^{-1}$) and $T$ the absolute temperature.

## Summary

(1) The reduction of selenious acid in hydrochloric acid by sulfur dioxide is a typical second order reaction with respect to selenious acid, while the reaction is of zero order with respect to sulfur dioxide because of the continuous passage of sulfur dioxide through a solution.

(2) The results obtained at 70, 60, 55 and 50°C ($a$=0.0184 mol./l., $[H^+]$=0.49 g. ion/l.) give a good Arrhenius plot, leading to the value of 24.5 kcal. $mol^{-1}$ for the energy of activation.

(3) The rate constant of this reaction under a certain condition can be evaluated by the general equation,

$$k_1 = 2.054 \times 10^{15} \times [H^+]^2 \exp(-E/RT)$$

where $[H^+]$ is hydrogen ion concentration, $E$, the energy of activation and $T$ absolute temperature.

*4 These experimental data are in good accordance with theoretical values (denoted by •) obtained from Eq. 2.

(4) The reduction of selenious acid in sulfuric acid, which will be published in a subsequent paper, is a reversible reaction. The above equation for the rate constant is utilized as a basic equation, in order to determine the rate constant in the forward direction of the reversible reaction.

The author wishes to express his sincere thanks to Dr. H. Negita of the Department of Chemistry, Hiroshima University, for his discussion and advice, and also he wishes to thank Mr. M. Kodama for his assistance.

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# *Kinetics of the Reduction of Selenious Acid by Sulfur Dioxide. II. Reduction in Acidic Solution with Sulfuric Acid**

By Keinosuke HAMADA

(Received Feburary 17, 1960)

This paper deals with the kinetics of the reduction of selenious acid in sulfuric acid by sulfur dioxide. Amelin and Yashke[1] investigated the reduction of selenious acid in concentrated sulfuric acid (60~80% by weight), and reported that the reaction was of first order with respect to selenious acid and to sulfur dioxide. The present author has studied the reduction of selenious acid by sulfur dioxide in dilute sulfuric acid, and has obtained different results from that obtained when concentrated sulfuric acid is utilized. The same method as that described in Part I[2] of this series was used. However, since it was found that the reaction in sulfuric acid was reversible, the method of measurements was improved by taking account of the equilibrium in the reversible reaction. The influences of temperature, initial concentration of selenious acid and hydrogen ion concentration on the reaction were investigated, and also general equations were derived for $k_2$*1 and $k_2'$ which were rate constants of the forward and reverse reactions.

## Experimental

**Materials.** — 0.736, 0.368 and 0.184 mol./l. aqueous solutions of selenious acid were prepared by dissolving extra pure reagent selenious acid in distilled water. Also prepared were 6.0, 4.5, 3.0 and 1.5% (by volume) sulfuric acid by diluting the first grade reagent sulfuric acid (s. g. about 1.84) with distilled water. pH*2 values were 0.08, 0.22, 0.38 and 0.62, and their hydrogen ion concentrations were evaluated to be 0.83, 0.60, 0.42 and 0.24 g. ion/l., respectively. The liquid sulfur dioxide was purchased.

**Measurements.** — This experiment was performed by means of the same procedures as those reported in Part I[2] of this series except that sulfuric acid was used in place of hydrochloric acid. However, since it was discovered that the reaction in sulfuric acid was reversible, the procedure suitable to this factor was adopted. That is, after the expected time for the reaction had elapsed, the precipitated selenium was filtered with a glass filter (IG-4)*3. Then the selenium was washed with dilute hydrochloric acid and water. Hereafter, the experimental procedures are the same as those in Part I[2] of this series.

## Results and Discussion

**Selenious Acid Concentration Dependence of the Reduction of Selenious Acid.** — Ten milliliters of the three selenious acid solutions were diluted to 200 ml. with 4.5% (by volume) sulfuric acid ($[H^+]=0.60$), the concentrations of the experimental solutions of selenious acid being 0.0092, 0.0184 and 0.0368 mol./l., respectively. These solutions were reduced by sulfur dioxide at constant temperature (60°C). Weights of precipitated selenium were converted into percentage completion, and the plot of the percentage completion against elapsed time (sec.) is shown in Fig. 1.

* Presented at the 13th Annual Meeting of the Chemical Society of Japan, Tokyo, April, 1960.

1) A. G. Amelin and E. V. Yashke, *Proc. Acad. Sci. U. S. S. R. Sec. Chem.*, **108**, 313 (1956); *Chem. Abstr.*, **51**, 54g (1957); *Chem. Zentr.*, **128**, 6688 (1957).

2) Part I: This Bulletin, **34**, 593 (1961).

*1 $k_2$ does not mean the rate constant of the second order reaction, but the rate constant of reaction in sulfuric acid.

*2 Measured by a pH-meter with 0.01 pH accuracy.

*3 Since the present reaction is reversible, diluting reactants with water can not be adopted to stop the process of the reaction. The effects of a reverse reaction appear conspicuously.

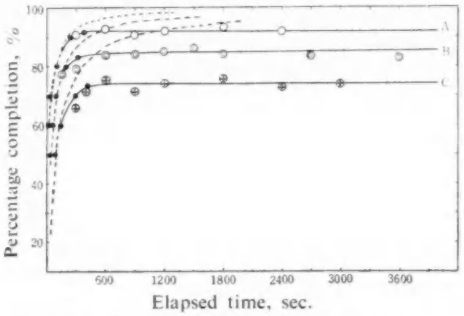


Fig. 1. $H_2SeO_3$ concn. dependence of the reduction of $H_2SeO_3$ at const. temp. (60°C) and const. $[H^+]$ (0.60 g. ion/l.).
○ 0.0368 mol./l. ◎ 0.0184 mol./l.
◉ 0.0092 mol./l. • calculated by Eq. 4.
Dotted lines: forward reaction with rate constant obtained from Eq. 1, when reverse reaction does not occur.

Each curve of Fig. 1 reaches an equilibrium, which is very different from the results in hydrochloric acid[2]. It is certain that the present reaction which comes to equilibrium is reversible[3].

The lines estimated from the experiment in the region below 60% completion of reaction are in good accordance with those obtained from Eqs. 1 and 2 based on only the forward reaction[2] (dotted lines).

Accordingly, the effect of the reverse reaction can be neglected in the region below 60% completion, where the reaction appears to be similar to the simple reaction in hydrochloric acid.

Provided that the reaction in sulfuric acid is of the second order with respect to selenious acid as it was in the case of hydrochloric acid, the rate constant $k_2$ for the forward reaction can be calculated by $t_{1/2}=1/(k_2a)$*1.

In the region below 60% completion, the author could not obtain any experimental data which could discriminate between curves $A_1$, $B_1$ and $C_1$. However, the value of $k_2$ in the reaction for curve $C_1$ is calculated to be 1.278 l. mol$^{-1}$ sec$^{-1}$ from $t_{1/2}=1/(k_2a)$, since the half time ($t_{1/2}$) is evaluated to be 85 sec. from the curve $C_1$ of Fig. 1, which is estimated from the experiment ($a=0.0092$ mol./l.).

The general equation for the rate constant of the reaction in hydrochloric acid was obtained as follows[2];

$$k_1=2.054\times10^{15}\times[H^+]^2\times\exp(-E/RT)$$
$$(E=24.5\ \text{kcal./mol.})$$

When the experimental conditions for curve $C_1$, 60°C and 0.60 g. ion/l., are substituted for $T$ and $[H^+]$ in the above equation, the rate constant can be calculated to be 0.0629 l. mol$^{-1}$ sec$^{-1}$. This value is far below the above-mentioned value (1.278 l. mol$^{-1}$ sec$^{-1}$), so it has to be multiplied by 20 in order to be in good accordance with the latter value. In this way, the general equation for rate constant $k_2$ of the forward reaction in sulfuric acid is expressed tentatively as follows:

$$k_2=20\times k_1$$
$$k_2=4.108\times10^{16}\times[H^+]\times\exp(-E/RT)$$
$$(E=24.5\ \text{kcal./mol.}) \qquad (1)$$

The values of $k_2$ estimated from the experiment in the reaction for curves $A_1$ and $B_1$ of Fig. 1 are in accordance with the ones calculated from Eq. 1.

The reverse rate constant $k_2'$ can be obtained by substituting the value of forward rate constant $k_2$, which is calculated from Eq. 1 in Eq. 3. When $k_2$ and $k_2'$ are substituted in Eq. 4, the parts of the curves in Fig. 1 are drawn theoretically. The curvatures obtained from the experiment are in good accordance with those drawn by the calculated values from Eq. 4.

From these facts it is concluded that the values of $k_2$ based on Eq. 1 are correct.

Eq. 1 is derived by assuming that the activation energy $E$ of the reaction in sulfuric acid is equal to the one in hydrochloric acid ($E=24.5$ kcal./mol.). However, the coefficient of 20 may be due to the difference of the activation energy in each case. Although the energy of activation could not be obtained experimentally, it will be possible for it to be obtained by calculation. The values of $k_2$ at 60, 50, 40 and 30°C are calculated with Eq. 1 to be 1.258, 0.400, 0.118 and 0.032 l. mol$^{-1}$ sec$^{-1}$, respectively. The line A of Fig. 3 shows the plotting of the logarithm of $k_2$ against the reciprocal of the absolute temperature. Each point falls upon a straight line. It follows from the slope of the straight line that the energy of activation is 22.5 kcal./mol. So, Eq. 1 is rewritten as follows:

$$k_2=2.054\times10^{15}\times[H^+]^2\times\exp(-E/RT)$$
$$(E=22.5\ \text{kcal./mol.}) \qquad (1')*5$$

The dotted lines in each figure are obtained from Eqs. 1 and 2,

$$t=p/\{k_2a(a-p)\}=x/\{k_2a(1-x)\}$$
$$(p=ax) \qquad (2)*6$$

3) S. Glasstone, "Elements of Physical Chemistry", Maruzen, Tokyo (1958), p. 600.

*4 Eq. 3 in Part I[2] of this series (as $n=2$).

*5 Eq. 1' is the same equation as Eq. 1. But, for the general equation of rate constant, the expression of Eq. 1' seems to be better than the one of Eq. 1.

*6 Eq. 2 in Part I[2] of this series (as $n=2$).

where $t$ is the elapsed time (sec.) of reaction, $p$ the reduced quantity of selenious acid (mol./l.) when time $t$ has elapsed, $x$ percentage completion (%) when time $t$ has elapsed, $k_2$ rate constant (l. mol$^{-1}$ sec$^{-1}$), and $a$ initial concentration of selenious acid (mol./l.).

The reversible reaction which is of the second order with respect to selenious acid can be expressed mathematically[3] by

$$-\mathrm{d}(a-p)/\mathrm{d}t=\mathrm{d}p/\mathrm{d}t=k_2(a-p)^2-k_2'p^2 \qquad (3)^{4)*7}$$

The solution of Eq. 3 is as follows, ($p=ax$)

$$t=\frac{2.303}{2a\sqrt{k_2k_2'}}\times\log\left|\frac{\{(k_2-k_2')x-k_2-\sqrt{k_2k_2'}\}/(k_2-k_2')x-k_2+\sqrt{k_2k_2'}}{(-\sqrt{k_2k_2'}-k_2)/(\sqrt{k_2k_2'}-k_2)}\right| \qquad (4)$$

The curvatures of the practical lines are drawn according to Eq. 4. Values of $k_2'$ in Eq. 4 can be obtained from Eq. 5.

As the reverse reaction occurs, selenium must be dissolved in dilute sulfuric acid. However, the purchased selenium is not dissolved in dilute sulfuric acid or in basic solution ($NH_4OH$)*8. This is inconsistent with the fact that the reduction of selenious acid in dilute sulfuric acid is a reversible reaction. This discrepancy can be solved by assuming that $\alpha$ selenium is dissolved in dilute sulfuric acid or in a basic solution, whereas $\beta$ selenium is not dissolved*8. The purchased selenium is dried at 100~105°C, and is of the $\beta$ form.

On the contrary, the selenium produced by reducing selenious acid below 99°C is of the $\alpha$ form, because the allotropic transition temperature of selenium from $\alpha$ to $\beta$ is 99°C[5].

At equilibrium of the reversible reaction, it is evident that $\mathrm{d}p_m/\mathrm{d}t=0$ in Eq. 3 where $p_m$ is the value of $p$ at equilibrium (the value of $p$ at equilibrium is equal to the maximum value of $p$). When $p$ is equal to $p_m(ax=ax_m)$, Eq. 5 can be derived from Eq. 3 as follows,

$$\mathrm{d}p/\mathrm{d}t=k_2(a-p_m)^2-k_2'p^2_m=k_2a^2(1-x_m)^2-k_2'a^2x_m^2=0 \qquad (5)$$

where $x_m$ is the maximum percentage completion at equilibrium. The values of $x_m$ obtained from Fig. 1 are 92, 85 and 74%, respectively. When the values of $x_m$ and $k_2$ (1.258 l. mol$^{-1}$ sec$^{-1}$) obtained from Eq. 1 are substituted in Eq. 5, then the values of $k_2'$ can be calculated to be 0.009, 0.039 and 0.155 l. mol$^{-1}$ sec$^{-1}$ for curves $A_1$, $B_1$ and $C_1$ in Fig. 1.

Table I shows the relation between the initial concentration of selenious acid, $a$, and the reverse rate constant, $k_2'$.
It is evident from Table I that $k_2'$ is inversely proportional to $a^2$.

TABLE I. RELATION BETWEEN $a^2$ AND $k_2'$

| $a$, mol./l. | $x_m$, % | $k_2$ | $k_2'$ | $a^2k^2\times10^{-5}$ |
|---|---|---|---|---|
| 0.0368 | 92 | 1.258 | 0.009 | 1.30 |
| 0.0184 | 85 | 1.258 | 0.039 | 1.33 |
| 0.0092 | 74 | 1.258 | 0.155 | 1.24 |

**Temperature Dependence of the Reduction of Selenious Acid.** — At constant initial concentration of selenious acid (0.0184 mol./l.) and hydrogen ion concentration (0.60 g. ion/l), selenious acid in sulfuric acid is reduced by sulfur dioxide at different temperatures, 60, 50, 40 and 30°C.

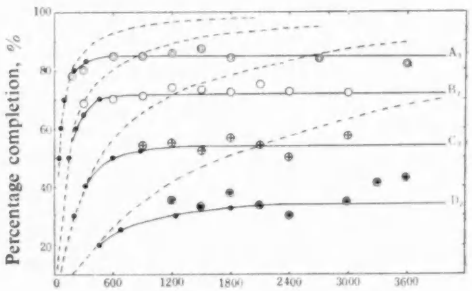


Fig. 2. Temp. dependence of the reduction of $H_2SeO_3$ at const. [$H_2SeO_3$] (0.0184 mol./l.) and const. [$H^+$] (0.60 g. ion/l.).
◎ 60°C ○ 50°C ⊕ 40°C ⊙ 30°C
• Calculated by Eq. 4.
Dotted lines: Ref. 2, Fig. 1

4) A. Wattilon and F. Grunderbeck, *Bull. soc. chim. Belges*, **65**, 657 (1956); *Chem. Abstr.*, **51**, 7103 (1957).

*7 Although the precipitated selenium coagulates gradually at a temperature above about 40°C in this experiment, the size of selenium particles prepared at the outset of the reaction is ultramicroscopic or electronmicroscopic. The very fine particles of selenium are dispersed by the passage of sulfur dioxide at the onset of the reaction. The reaction in the reverse direction is one where the dissolving of the precipitated selenium on its surface takes place. When $k_s$ is a rate constant for dissolving the solid and $S$ is the constant dependent on the surface of the solid, $k_sSp^2$ expresses a rate of the reverse reaction. If $S$ is constant under the present experimental conditions, $k_sSp^2$ can be expressed by $k_2'p^2$ in Eq. 3. From Figs. 1, 2 and 4, it is seen that the higher the temperature, greater hydrogen ion concentration and initial concentration of selenious acid are, the better are the experimental data in accordance with Eq. 3. If $S$ is variable under all experimental conditions, Eq. 3 can not be derived.

*8 Eq. 6 shows that the lower the hydrogen ion concentration, the higher is the value of $k'_2$ (rate constant of reverse reaction), i.e., selenium is dissolved in basic solution more easily than in acidic solution. In fact, selenium produced by reducing selenious acid at 60°C disappears by adding basic solution[2] ($NH_4OH$), but selenium dried over 100°C does not dissolve in basic solution.

5) Roger Dolique et al., *Bull. soc. chim. France, Mém.* [5], **10**, 231 (1943); *Chem. Abstr.*, **38**, 6156-8 (1944).

The results are shown in Fig. 2, where the precipitated selenium is converted into percentage completion. The values of $k_2$ at 60, 50, 40 and 30°C are calculated with Eq. 1 to be 1.258, 0.400, 0.118 and 0.032 l. mol$^{-1}$ sec$^{-1}$, respectively. The values of $x_m$ at the above temperature can be obtained from Fig. 2, and they are 85, 72, 54 and 34%, respectively. Making these substitutions for $k_2$ and $x_m$ in Eq. 5, the values of $k_2'$ at each temperature can be calculated to be 0.039, 0.060, 0.086 and 0.121 l. mol$^{-1}$ sec$^{-1}$.

Line B of Fig. 3 shows the plotting of the logarithm of $k_2'$ against the reciprocal of the absolute temperature ($1/T$). It is evident that experimental points fall upon a straight line. The relation between the rate constant of reverse direction and the temperature can be derived from the straight line B in Fig. 3 as follows.

$$k_2' \propto \exp(-E/RT)$$

The energy of activation $E$ can be calculated to be $-8.06$ kcal./mol. from the slope of the line B in Fig. 3.

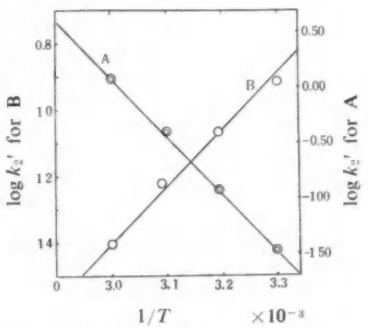


Fig. 3. Arrhenius' plot of the forward and reverse reaction.

**Hydrogen Ion Concentration Dependence of the Reduction of Selenious Acid.** — At constant initial concentration of selenious acid (0.0184 mol./l.), constant temperature (60°C) and various hydrogen ion concentrations (0.83, 0.60 and 0.042 g. ion/l.), selenious acid in sulfuric acid was reduced by sulfur dioxide.

The results are shown in Fig. 4, where precipitated selenium is converted into a percentage completion. The values of $k_2$ and $k_2'$ can be calculated from Eqs. 1 and 5, (see Table II).

From Table II, the rate constant of reverse direction, $k_2'$, is inversely proportional to the square of hydrogen ion concentration, $[H^+]^2$. According to the above-mentioned selenious acid concentration, temperature and hydrogen ion concentration dependence of the reverse

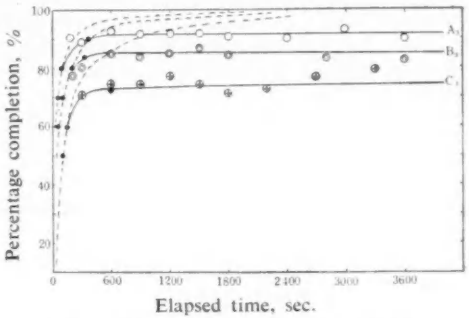


Fig. 4. $[H^+]$ dependence of the reduction of $H_2SeO_3$ at const. $[H_2SeO_3]$ (0.0184 mol./l.) and const. temp. (60°C).
○ 0.83 g. ion/l. ◎ 0.60 g. ion/l.
⊕ 0.42 g. ion/l. • Calculated by Eq. 4.
Dotted lines: Ref. Fig. 1

TABLE II. RELATION BETWEEN $k_2'$ AND $[H^+]$

| $[H^+]$ | $k_2$ | $x_m$, % | $k_2'$ | $[H^+]^2$ | $k_2' \times [H^+]^2$ ($\times 10^{-3}$) |
|---|---|---|---|---|---|
| 0.83 | 2.408 | 91.5 | 0.021 | 0.689 | 14.33 |
| 0.60 | 1.258 | 85.0 | 0.039 | 0.369 | 14.04 |
| 0.42 | 0.617 | 74.0 | 0.076 | 0.176 | 13.37 |

reaction, the general equation for the reverse rate constant $k_2'$ can be derived as follows:

$$k_2' = 2.413 \times 10^{-11} \times \{1/(a^2[H^+]^2)\} \times \exp(-E/RT) \qquad (6)$$

where $a$ is the initial concentration of selenious acid, $[H^+]$ hydrogen ion concentration, $E$ activation energy ($-8.06 \times 10^3$ kcal./mol.), $R$ the gas constant and $T$ the absolute temperature.

Also, the data of curve $B_1$ in Fig. 1, curve $A_2$ in Fig. 2 and curve $B_3$ in Fig. 3 are adopted for the above Eq. 6.

**Relation among Rate Constant, Maximum Percentage Completion and Initial Concentration of Selenious Acid.**—Fig. 5 shows the plotting maximum percentage completion $x_m$ against

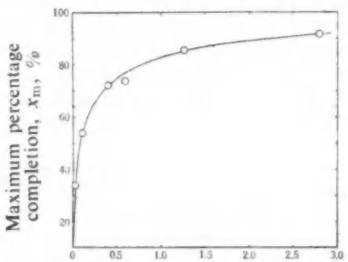


Fig. 5. Plot of maximum percentage ($x_m$) against forward rate constant ($k_2$).

forward rate constant $k_2$ at the constant initial concentration of selenious acid (0.0184 mol./l.). The experimental equation which expresses the relation between $x_m$ and $k_2$ can be derived from Fig. 5 by

$$x_m = 0.828 \times k_2^{0.114} \quad (\text{at } a = 0.0184 \text{ mol./l.}) \quad (7)$$

When the consideration of initial concentration of selenious acid $a$ is taken into Eq. 7, the relationship between $k_2$, $x_m$ and $a$ can derived as follows,

$$x_m = 1.306 \times (k_2 \cdot a)^{0.114} \quad (8)$$

**Summary**

(1) The reduction of selenious acid in sulfuric acid by sulfur dioxide is a reversible reaction, because the reaction has an equilibrium and the process of the reaction is in good accordance with the equation which expressed mathematically the reversible reaction, that is,

$$-d(a-p)/dt = dp/dt = k_2(a-p)^2 - k_2'p^2$$

(2) Up to the present time the rate constant $k_2$ of the forward reaction was derived by substitution of the experimental data for $x_m$ in the following equation,

$$k_2 = \{2.303x_m/2a(x_m-1)t\} \times \log[(x-x_m)/\{(2x_m-1)x-x_m\}]$$

The general equation for $k_2$, which does not depend on $x_m$, has been obtained as follows,

$$k_2 = 2.054 \times 10^{15} \times [H^+]^2 \times \exp(-E/RT)$$
$$(E = 22.5 \text{ kcal./mol.})$$

The rate constant $k_2'$ of the reverse reaction can be calculated by

$$k_2' = 2.413 \times 10^{-11} \times \{1/(a^2[H^+]^2)\} \times \exp(-E/RT) \quad (E = -8.06 \text{ kcal./mol.})$$

(3) It has not previously been reported that $\alpha$ selenium is dissolved in dilute sulfuric acid (below 85% by weight), as shown by the present experimental procedure.

(4) The results obtained from this study are useful in the recovery and refinining of selenium. Then application to the recovery and refining of selenium will be expressed in another succeeding paper.

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# *Kinetics of the Reduction of Selenious Acid by Sulfur Dioxide. III. Application to Recovery and Purification of Selenium in Sulfuric Acid Works*

By Keinosuke HAMADA

(Received March 30, 1960)

The greater part of the starting materials for the productions of selenium consists of an anode-slime deposited in the electrolytic refining of copper and a sludge containing selenium recovered in the manufacturing process of sulfuric acid. The latter is called sulfuric acid sludge.

The reaction of selenious acid by sulfur dioxide was found to be a reversible reaction in sulfuric acid. The general equation for the rate constant of the forward reaction and the relation between the rate constant and the maximum percentage completion (maximum yield) were derived in the previous paper[1].

A great deal of sludge has recently been recovered from the mist acid which is a by-product of the manufacture of sulfuric acid, and a very simple and economical method of purification of selenium has been found by means of the application of the experimental results[1].

**Application to the Recovery of Selenium in the Mist Acid.**—A schematic diagram of the contact process for manufacturing sulfuric acid is shown in Fig. 1. Generally pyrites have about 12.6 parts of selenium per million[2] of pyrites. When pyrite is roasted, the selenium in the

1) Part II; This Bulletin, **34**, 596 (1961).
2) T. Tsuge et al., *J. Agr. Chem. Soc. Japan (Nippon Nogei-Kagaku Kaishi)*, **23**, 421 (1950).

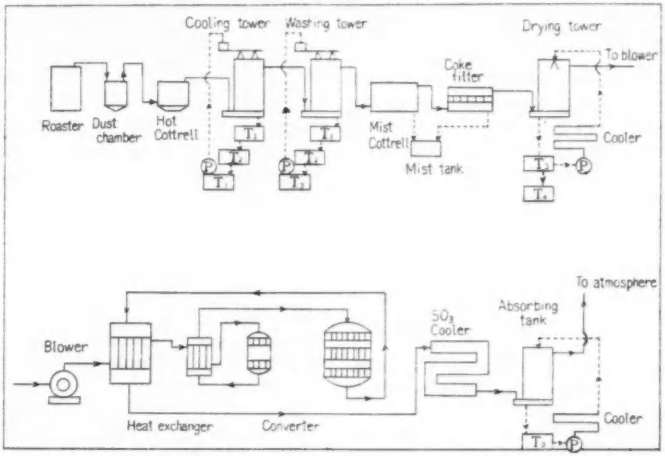


Fig. 1. Schematic diagram of contact process of sulfuric acid.

$T_1$: Cooling tank $T_4$: Storage tank →— Gas
$T_2$: Precipitating tank Ⓟ: Pump →-- Acid
$T_3$: Pump tank

pyrite is oxidized to selenium dioxide. The part of the selenium dioxide is dissolved in the mist acid*, which is excluded from gas by a mist Cottrell and a coke filter, and is brought into a mist tank. The concentration of the mist acid is about 15° Bé (s. g. 1.115) while the acid is saturated with sulfur dioxide. Nevertheless, a large quantity of selenious acid exists in mist acid without being reduced to selenium. This fact can easily by explained according to the results of Part II[1] of this series, as follows. The reaction of selenious acid with sulfur dioxide in sulfuric acid is reversible, and the rate constant of the forward reaction, $k_2$, is expressed according to the following equation:

$$k_2 = 2.054 \times 10^{15} \times [H^+]^2 \times \exp(-E/RT) \quad (E = 22.5 \text{ kcal./mol.}) \quad (1)$$

The equation which expresses the relation among rate constant, $k_2$, maximum percentage completion, $x_m$, and initial concentration of selenious acid, $a$, is as follows:

$$x_m = 1.306 \times (k_2 \cdot a)^{0.114} \quad (2)$$

In these equations, $[H^+]$ is hydrogen ion concentration, $T$ absolute temperature of solution, $E$ the energy of activation, $R$ the gas constant and $a$ initial concentration of selenious acid. It is evident that maximum yield, $x_m$, depends heavily on temperature at the constant $[H^+]$ and $a$, according to Eqs. 1 and 2. When the mist acid is heated up to the boiling point, selenium can be precipitated. After heating the mist acid, the selenium content in the mist acid is found to be about 0.00015 mol./l. Ninety-five per cent of selenium in the mist acid can be recovered by only heating the mist acid. Selenium sludge gained from the mist acid has a high content of selenium (about 80%), and a great deal of sludge can be recovered each day, making sludge a useful and plentiful starting substance for the isolation of selenium.

**Application to the Purification of Selenium.**—Up to the present time, many studies[3-33]

* The mist acid has about 0.003 mol. selenious acid per liter.

3) Z. Littmann, *Z. angew. Chem.*, **19**, 1039 (1906).
4) N. Chikashige et al., Brit. Pat. 134536 (1919).
5) J. Sugie, *Osaka Ind. Lab.*, **1**, No. 1, 1 (1920).
6) T. Shimoi et al., Japan. Pat. 3629 (1920).
7) S. Sugie, *J. Japan Ceram. Assoc.*, **343**, 226 (1921).
8) W. Stahl, *Chemiker-Ztg.*, **50**, 280 (1926).
9) Z. Littmann, ibid., **50**, 704 (1926).
10) A. A. Borkovski et al., *Zavodskaya Lab.*, **3**, 306 (1934); *Chem. Abstr.*, **29**, 1739 (1935).
11) A. R. Lindblad, Brit. Pat. 423084 (1935); Fr. Pat. 777857 (1935); Ger. Pat. 641714 (1937).
12) O. C. Martin et al., U. S. Pat. 2039256 (1936).
13) F. W. Heberlein, Can. Pat. 364133 (1937).
14) C. W. Clark et al., *Am. Inst. Mining Met. Engrs., Tech. pub.*, **982**, 22 (1938).
15) H. C. Dudley, U. S. Pat. 2111112 (1938).
16) M. S. Belskaya, Russ. Pat. 58836 (1941).
17) N. R. Bierly, U. S. Pat. 2349697 (1944).
18) C. W. Clark, U. S. Pat. 2409835 (1946).
19) A. J. Philip et al., U. S. Pat. 2413374 (1946).
20) N. S. Artamonov, U. S. S. R. Pat. 66128 (1946).
21) D. Gardner, U. S. Pat. 2414295 (1947).
22) M. C. Bloom, U. S. Pat. 2414438 (1947).
23) N. V. Philips, Fr. Pat. 930184 (1948).
24) A. Voige et al., Ger. Pat. 800860 (1950).
25) T. Sawaya, Japan. Pat. 18 (1950).
26) K. Krebs, Brit. Pat. 644743 (1950).
27) Y. Terasaki, Japan. Pat. 2560 (1952).
28) N. A. Vaarro, Span. Pat. 207021 (1954).
29) T. Tamura, Japan. Pat. 7052 (1955).
30) K. Okamoto, Japan. Pat. 3508 (1955).
31) N. Imai et al., Japan. Pat. 3108 (1956).
32) Y. E. Lebedeff et al., U. S. Pat. 2775509 (1956).
33) S. Ato et al., *Repts. Sci. Research Inst. (Japan)*, **32**, 27 (1956).

have been performed concerning the purification of selenium, and each method of purification of selenium has had its own characteristics.

In the purification of sulfuric acid sludge, the Stahl[5] and Littmann[5] method was found to be the most suitable. However, the method has some difficulty, the yield is relatively lower (around 85%). The present author has noticed that the yield depended largely on the hydrogen ion concentration and temperature according to Eqs. 1 and 2. Therefore, these two factors were taken into account for their method[8,9] as described subsequently.

## Experimental

A great success has been attained in the purification of selenium on the industrial scale by enlarging the experimental procedures. Therefore, the process on an industrial scale will now be described in some detail. Figure 2 shows the schematic diagram of the plant for purification of sulfuric acid sludge according to the new method.

The dried sludge is brought into a reacting vessel, and 20 l. of fuming sulfuric acid (23%) per 1 kg. pure selenium in the sludge is added to the vessel.

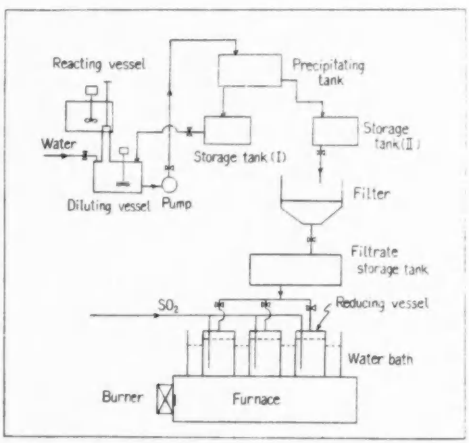


Fig. 2. Schematic diagram of purification plant of selenium.

These mixtures are agitated for two hours with a stirrer. The selenium in the sludge is changed to green selenium anhydro-sulphate ($SeSO_3$) according to the following reaction:

$$Se + H_2SO_4 \cdot SO_3 = SeSO_3 + H_2SO_4$$

Then, 2 l. of nitric acid (62% by weight) per 1 kg. pure selenium in the sludge is added to this green solution, and agitation is continued for one additional hour.

The temperature is increased up to about 120°C, and a yellow solution of selenious acid results as follows.

$$SeSO_3 + 4HNO_3 = H_2SeO_3 + H_2SO_4 + 4NO_2$$

The mixture containing selenious acid is slowly dropped into a diluting vessel, to which 50 l. of water per 1 kg. pure selenium in the sludge has previously been added. The temperature of the solution is elevated up to approximately 140°C, by the heat of the dilution of the fuming sulfuric acid. The excess of nitric acid is released owing to the high temperature. Moreover, 20 l. of water per 1 kg. pure selenium is added to the above solution.

The mixtures in the diluting vessel are pumped up to a precipitating tank, and cooled to the chamber temperature. Solid materials in solution, of course, settle down in this tank. The supernatant is brought into a storage tank (I), and subsequently sent to a filter. The filtrate is introduced into reducing vessels via a filtrate storage tank, and reduced to selenium by some previously water-washed sulfur dioxide (about 6%) used in the manufacture of sulfuric acid. When the solution of selenious acid is reduced, it is kept at bout 70°C*1 in a water bath.

The selenium precipitated in the reducing vessel is removed, washed by water till all traces of sulfuric acid disappear and dried in an air bath at 110°C or lower. The waste solution is 35% (by weight) sulfuric acid, and this solution can be utilized elsewhere in industry.

## Results

The purpose of the present study is to find the most suitable method for manufacture of selenium that meets the minimum commercial requirements in the sulfuric acid works.

A 92% yield*2 has been secured and the purity of 99.9% has been obtained according to this new method. Table I shows a few

TABLE I. DATA OF ANALYSIS OF PURIFIED Se AND RAW MATERIALS

| | Se, % | Fe | Si | Te | Hg | As | Ag | Pb |
|---|---|---|---|---|---|---|---|---|
| Purified Se (A) | 99.94 | w | w | www | s | nil | ww | nil |
| Raw material (A) | 29.63 | ss | s | s | s | ww | s | ss |
| Purified Se (B) | 99.97 | w | w | www | w | nil | ww | nil |
| Raw material (B) | 88.99 | ss | s | s | w | ww | s | ss |

w, weak; ww, very weak; www, trace; s, strong; ss, very strong.

*1 It is evident according to Eqs. 1 and 2, that the higher the temperature of the solution is, the greater the yield is. However, the particles of selenium separated at high temperature (about 80°C) are very small. At about 70°C, most particles of the precipitated selenium can pass through a 80~100 mesh sieve, and so they meet commercial requirements. The difference of yield between those at 70°C and at 80°C can hardly be appreciated by the present experiments.

*2 Yield of conventional methods is between 80 and 90%.

examples of analysis*3 of selenium purified by the new method and raw materials.

Table I expresses the relative strength of the lines of emission spectra, except the data for selenium. A remarkable result is shown in Table I, namely, tellurium can be removed without any special effort, but on the contrary, most of the mercury remains in the purified selenium.

## Discussion

Selenium in mist acid can be recovered by heating the acid according to the results of Part II[1] of this series.

By improving the Stahl[8] and Littman[9] method according to the results of Part II[1], the simple method for purification of selenium has been found. It was already mentioned in the present paper that this method had many virtues. Especially, it is interesting to note that tellurium can be excluded from the purified selenium without any special steps. According to conventional methods, some special steps were necessary in order to exclude impurities; for example, tellurium. These special processes are: i) using hydrochloric acid[10], ii) ion-exchange resin[34], and iii) distillation[11,15,33,35-39,42]. But it is unnecessary to include any provisions for removal of tellurium in the present method*4[,40,41].

It is the defect of this method that the purity of four nine can not be secured, although that of three nine can be secured. This seems to be caused by the mercury as an impurity.

The author wishes to thank Dr. H. Negita of the Department of Chemistry, Hiroshima University, for the discussion, and also to express hearty thanks to the Factory Manager, E. Yamashita, for the K. Chemical Company of the application of the author's experimental results[1] to the purification of selenium on an industrial scale and the permission to publish the industrial method, also to the staffs of the Department of Sulfuric Acid and Laboratory in the company for their advice and help.

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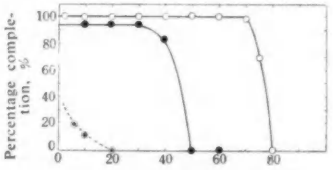


Fig. 3. Reduction of tellurous acid by $SO_2$.
◉ In acidic soln. with $H_2SO_4$
● In acidic soln. with ($H_2SO_4$+10cc. HCl(s. g. 1.18))
○ In acidic soln. with HCl

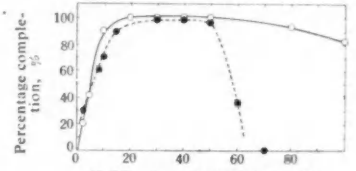


Fig. 4. Reduction of selenious acid by $SO_2$.
○ In acidic soln. with $H_2SO_4$
● In acidic soln. with HCl

*3 Selenium is determined by means of gravimetric analysis, while others were determined by spectrochemical analysis.

34) F. Aoi, This Bulletin, **26**, 480 (1953).
35) H. Bode, *Z. anal. Chem.*, **134**, 100 (1951).
36) A. I. Gaev, Russ. Pat. 51200 (1937).
37) N. S. Polvektov, *Microchemie*, **15**, 32 (1934).
38) S. T. Volkov, *Zavodskaya Lab.*, **5**, 1429 (1936); *Chem. Abstr.*, **31**, 6130 (1937).
39) V. K. Zemel, ibid., **5**, 1443 (1936).
40) E. M. Müller, *Z. physik. Chem.*, **100**, 346 (1922).
41) T. L. Pökrovskaya, *Zavodskaya Lab.*, **7**, 15 (1938); *Chem. Abstr.*, **32**, 4101 (1938).
42) T. Takei et al., *Repts. Sci. Research Inst. (Japan)*, **26**, 234 (1950).

*4 It is believed that, tellurium is excluded based on this fact, the higher the concentration of sulfuric acid, the smaller is the rate constant of reduction of tellurous acid in sulfuric acid. This can be guessed by the following simple, qualitative experiment. A solution of tellurous acid of 0.01 mol. per 200 ml. sulfuric acid of many kinds of concentrations were prepared, and left overnight at chamber temperature after being saturated with sulfur dioxide. Fig. 3 shows the plot of the tellurium precipitated (percentage completion) against each concentration of sulfuric acid. One can see that when the concentration of sulfuric acid is above 20% (by volume), tellurium can not be precipitated. Fig. 4 is the same plot as in the case of selenious acid for comparison with Fig. 3.

# *The Relation between Reactivity and Selectivity*

By Yoshiro OGATA and Iwao TABUSHI

(Received July 12, 1960)

Brown and his coworkers have pointed out the existence of the linear relation between the logarithm of the para partial rate factor of toluene, $\log p_f$, which they called a measure of activity of reagent and the selectivity factor which is expressed as the logarithm of ratio of para vs. meta partial rate factor, $\log(p_f/m_f)$[1]. As they have mentioned, the relation can be derived from the Hammett equation and is expressed as

$$\log p_f = \frac{\sigma_p}{\sigma_p - \sigma_m} \log(p_f/m_f) \qquad (1)$$

However, the term of $\log p_f$ is not the reactivity, but the distribution of a given reagent between benzene and toluene, or intermolecular selectivity and it is not surprising that the intermolecular selectivity is proportional to the intramolecular selectivity, $\log(p_f/m_f)$.

The reactivity of a reagent should be expressed as a value related to the rate constant for the reaction between a standard substance and the reagent at a standard condition or $k_0$. The value of $k_0$, however, depends on the reaction mechanism, the concentration of the actual attacking species, the environment and conditions. Hence it is difficult to compare the value of $k_0$ at a standard condition. Nevertheless, as shown in Table I, A-1 and A-2 the qualitative parallelism is sometimes observed between $k_0$ and the absolute value of $\rho$ or the sensitivity of the rate to the change of substituent in closely related reactions[1c].

If frequency factors are constant, the relative

TABLE I

(A) COMPARISON OF DIFFERENT ATTACKING REAGENTS

A-1) Aromatic alkylation

| Reaction | Solvent | $-\rho$ | $\log k_0$ l. mol$^{-1}$ sec$^{-1}$ | Ref. |
|---|---|---|---|---|
| ArH + MeBr, $AlCl_3$ | 1,2,4-$Cl_3C_6H_3$ | 3.64 | −2.444 | 6 |
| ArH + MeBr, $GaBr_3$ | ArH | 3.06 | −1.301 | 7 |
| ArH + EtBr, $GaBr_3$ | ArH | 2.66 | −0.799 | 7 |
| ArH + *i*-PrBr, $GaBr_3$ | ArH | 2.54 | +2.505 | 7 |

A-2) Electrophilic halogenation at 25 C (X; H or $CH_3$)

| Reaction | $-\rho$ | $\log k_0$, l. mol$^{-1}$ sec$^{-1}$ | Ref. |
|---|---|---|---|
| $C_6H_5X + HClO$ | 7.77 | −3.380 | 8 |
| $C_6H_5X + HBrO$ | 6.05 | −0.234 | 9 |

A-3) Electrophilic addition[10]

| Reaction | Products | |
|---|---|---|
| | 1-Halo-compound | 2-Halo-compound |
| $CH_2=CH-CH_3 + HClO$ | $ClCH_2CHOHCH_3$ (90%) | $CH_2OHCHClCH_3$ (10%) |
| $CH_2=CH-CH_3 + HCl$ | None | $CH_3CHClCH_3$ |
| $CH_2=CH-CH_2Cl + HClO$ | $ClCH_2CHOHCH_2Cl$ (30%) | $CH_2OHCHClCH_2Cl$ (70%) |
| $CH_2=CH-CH_2Cl + HCl$ | None | $CH_3CHClCH_2Cl$ |

(B) COMPARISON OF DIFFERENT SUBSTRATES

Second-order rate constants of chlorination[11], l. mol$^{-1}$ min$^{-1}$

| R | *p*-Me | H | *m*-$NO_2$ |
|---|---|---|---|
| 1. R-$C_6H_4CH=CHCOPh$ | 800 | 61 | 0.23 |
| 2. R-$C_6H_4CH=CH-CO_2H$ | 103 | 4.9 | 0.011 |
| $k_1/k_2$ | 7.76 | 12.4 | 20.9 |

1) a) H. C. Brown and K. L. Nelson, *J. Am. Chem. Soc.*, **75**, 6292 (1953).
b) H. C. Brown and W. H. Bonner, ibid., **76**, 605 (1954).
c) H. C. Brown and C. W. McGary, Jr., ibid., **77**, 2300 (1955).
d) H. C. Brown and C. R. Smoot, ibid., **78**, 6255 (1956).
e) L. M. Stock and H. C. Brown, ibid., **81**, 3233 (1959), **82**, 1942 (1960).

rate constant of substituted and unsubstituted reactants is expressed as

$$\ln(k/k_0) = -\frac{\Delta H^{\ddagger} - \Delta H_0^{\ddagger}}{RT} = \sigma\rho \qquad (2)$$

Hence it is rational that the absolute value of $\rho$ with constant $\sigma$ decreases with an increase of temperature[2] which accompanies an increase of the rate constant in the same reaction series. Furthermore, it is supposed from Eq. 2 that the absolute value of $\Delta H^{\ddagger} - \Delta H_0^{\ddagger}$ approaches zero, when both $\Delta H^{\ddagger}$ and $\Delta H_0^{\ddagger}$ approach zero or $k_0$ becomes very large. Therefore, the $\rho$ value with constant $\sigma$ tends to decrease with an increase of $k_0$ under this limitation. Thus the very fast reaction such as protonation have a constant value of rate constants ($3\times 10^{10}$ l. mol$^{-1}$ sec$^{-1}$ at 18~30°C) or the $\rho$ value of zero[5].

The selectivity may be expressed with either intramolecular selectivity, i.e., orientation, or intermolecular selectivity, i.e., relative rate. Since the former selectivity is proportional to the latter in aromatic compounds[4,5], as shown in Eq. 1, the reactivity-selectivity relation can be tested with any of these selectivities.

Table I shows A) comparison of different attacking reagents and B) comparison of some groups of substrates with different reactivities.

2) H. H. Jaffé, *Chem. Revs.*, **53**, 191 (1953); H. C. Brown and C. W. McGary, Jr., *J. Am. Chem. Soc.*, **77**, 2306 (1955).
3) R. P. Bell, *Quart. Revs.*, **13**, 169 (1959).
4) L. M. Stock and H. C. Brown, *J. Am. Chem. Soc.*, **81**, 2320 (1959).
5) The same is true with aliphatic compounds in which polar effect alone is important.
6) H. Jungk, C. R. Smoot and H. C. Brown, *J. Am. Chem. Soc.*, **78**, 2185 (1956).
7) H. C. Brown and H. Jungk, ibid., **77**, 5584 (1955).
8) P. B. D. de la Mare, J. T. Harvey, M. Hassan and S. Varma, *J. Chem. Soc.*, **1958**, 2756.
9) P. B. D. de la Mare and J. T. Harvey, ibid., **1956**, 36.
10) J. R. Shelton and L. Lee, *J. Org. Chem.*, **25**, 907 (1960). More reactive HClO adds less regularly to substituted ethylenes in comparison with less reactive HCl.
11) P. B. D. de la Mare, *Quart. Revs.*, **3**, 126 (1949).


## Summary

The proportionality between $\log p_f$ and $\log(p_f/m_f)$ reported by Brown[1] seems to express the proportionality between inter- and intramolecular selectivities. The standard rate constant $k_0$ may be a measure for the reagent activity; the parallelism between $1/k_0$ and $|\rho|$ or selectivity is observed in very limited reactions.



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# *Acid-Base Property and Metal Chelate Formation of 4-(2-Pyridylazo)-resorcinol**


By Toschitake IWAMOTO



(Received January 7, 1960)


4-(2-Pyridylazo)-resorcinol (PAR) has recently been suggested as a water-soluble metal indicator for the EDTA-titration of lead and other metal cations in place of 1-(2-pyridylazo)-2-naphthol (PAN)[1]. The latter forms a colloidal suspension when dissolved in water in the pH range 2 to 13[2], and this fact is one of the disadvantages of the reagent in aqueous systems. The use of PAR as a color reagent in colorimetric analysis[3] and as a metal indicator in precipitation titration[4] and in chelatometric titration[5] has been proposed, all of which is based on the formation of stable colored chelates of PAR with various heavy metals such as lead, cobalt and uranium.

The present paper concerns the acid dissociation of PAR, its chelate formation with some metal cations in aqueous solutions, the stability constant of copper(II)-PAR chelate and the comparison between PAR and PAN as analytical reagent.

The absorption spectra of PAR in aqueous

* Presented partly at the 13th Annual Meeting of the Chemical Society of Japan, Tokyo, April, 1960.
1) P. Wehber, *Z. anal. Chem.*, **158**, 10 (1957); **167**, 186 (1958).
2) B. F. Pease and W. B. Williams, *Anal. Chem.*, **31**, 1044 (1959).
3) F. H. Pollard, P. Hanson and W. J. Geary, *Anal. Chim. Acta*, **20**, 26 (1959).
4) R. Püschel, E. Lassner and R. Scharf, *Z. anal. Chem.*, **163**, 104, 344 (1958); **165**, 401 (1959).
5) E. J. Langmyhr and H. Kristiansen, *Anal. Chim. Acta*, **20**, 524 (1959).

solution at various pH values have been examined, the acid dissociation constants determined by pH-titration and colorimetric method. The composition of the metal chelates of PAR with tervalent iron, bivalent cobalt, nickel, copper, zinc, cadmium, mercury and lead has been determined with the aid of the continuous variation method[6] and the stability constant of copper(II)-PAR chelate determined potentiometrically by pH-titration; its utility in chelatometric analysis was discussed.

## Experimental

The PAR used in this study was a sample for test supplied by Dojin Pharmaceutical Laboratories, Kumamoto, Japan.

Found: C, 61.4; H, 4.5; N, 18.7; Calcd. for $C_{11}H_9O_2N_3$: C, 61.1; H, 4.2; N, 19.5[7].

PAR in free acid form is readily soluble in an aqueous alkaline solution. Solubility in water at 10°C was found to be only 5 mg./100 ml.

4-Benzeneazoresorcinol was kindly given by Dr. Yoshio Matsunaga in our laboratory.

A solution of $10^{-2}$ M potassium hydroxide was prepared by direct dissolution of metallic potassium (E. Merck) in deionized water in a current of nitrogen, and standardized against $1.007_4\times10^{-2}$ M hydrochloric acid. The standard solution of the

Fig. 1. Absorption spectra of PAR.
$5\times10^{-5}$ M: 1 cm. silica cell (Cary)

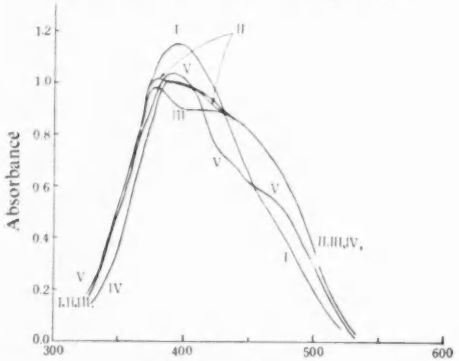



Fig. 1a. Absorption spectra of PAR in acid solutions.
I: 4.7 N $HNO_3$
II: 3.2 N $HNO_3$
III: 1.6 N $HNO_3$
IV: 0.1 N $HNO_3$
V: pH 3, acetate buffer (0.1 M $KNO_3$)

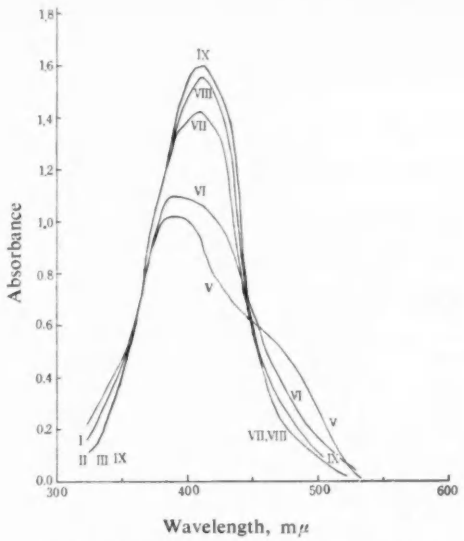



Fig. 1b. Absorption spectra of PAR in neutral solutions.
V: pH 3, acetate buffer
VI: pH 5, acetate buffer
VII: pH 7, phosphate buffer } (0.1 M $KNO_3$)
VIII: pH 9, borax buffer
IX: pH 11, 0.001 N NaOH

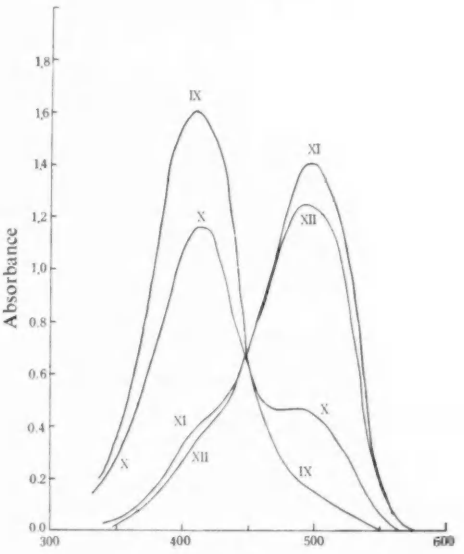



Fig. 1c. Absorption spectra of PAR in alkaline solutions.
IX: 0.001 N NaOH } (0.1 M $KNO_3$)
X: 0.01 N NaOH
XI: 0.1 N NaOH
XII: 1 N NaOH

6) Y. Shibata, T. Inouye and Y. Nakatsuka, *J. Chem. Soc. Japan (Nippon Kwagaku Kwaishi)*, **42**, 983 (1921); R. Tsuchida, This Bulletin, **10**, 27 (1933). Cf. P. Job, *Ann. chim.*, [10] **9**, 113 (1928).

7) Elementary analysis was performed by Mr. Shozo Masuda in our department. The PAR might contain some impurities (cf. Refs. 2 and 3). The purity of the PAR calculated from the content of nitrogen 18.7/19.5=0.96, agreed with that (0.94) determined by photometric titration with a copper nitrate solution.

acid was prepared by passing a known amount of potassium chloride solution through a column of cation-exchange resin in H-form (Diaion SK #1, analytical grade).

All the other chemicals were of reagent grade, and all metal salts were used as nitrates. Acetate, phosphate and borax buffer, nitric acid, potassium hydroxide and sodium hydroxide solution were used to control the pH. By photometric titrations[7a] with $1.00\times10^{-4}$ M copper nitrate solution, the PAR solutions were standardized after suitable dilution whenever necessary.

The absorption spectra were measured by a Cary Model 11 and a Shimadzu QB-50 spectrophotometer and the colorimetric measurements were done by a Hirama IIb filter electrophotometer. For pH-titrations and pH measurements a Denkishiki DG pH meter equipped with a glass and a calomel electrode was used; the measurements were carried out in a thermostat regulated at $25\pm0.2$°C by circulating water from another large thermostat. During titration the solution was stirred magnetically and bubbled with nitrogen gas through a capillary.

## Results and Discussion

**Acid Dissociation of PAR.**—The absorption spectra of aqueous solutions of PAR depend on the pH values as shown in Fig. 1. The spectra in acid solutions have somewhat complicated aspects which may be caused by the presence of pyridinium form or azo-protonated forms as in case of PAN[2] and some azobenzene derivatives[8]. It can be suggested that an undissociated form a, two kinds of the dissociated forms b and c, and one-protonated form d exist in neutral and alkaline solutions. As the degree of acid dissociation of *o*-hydroxyl group may be lower than that of *p*-hydroxyl group through an intramolecular hydrogen bond formation, the absorption maxima at 390, 410 and 490 mμ can be assigned to a, b and c, respectively, and the broad shoulder from 400 to 470 mμ to d. The existence of these dissociation stages in neutral and alkaline solutions can be supported by similar study on 4-benzeneazoresorcinol. As shown in Fig. 2, in the neutral solution the spectrum has a doublet of 375 and 410 mμ (Curve I)[9]. In the weakly alkaline solutions the absorption maximum shifts to 430 mμ (Curves II and III) and in the more alkaline solution the maximum further shifts to 475 mμ and shows a shoulder at 390 mμ (Curve IV). These properties are analogous to those of PAR.

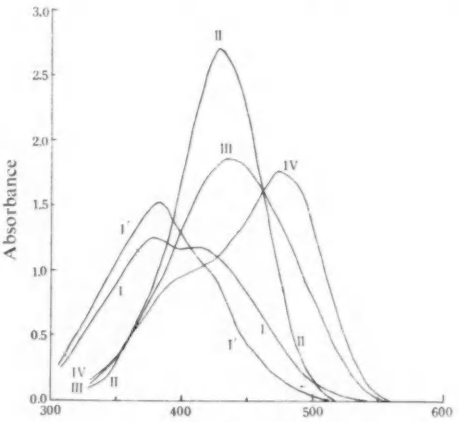
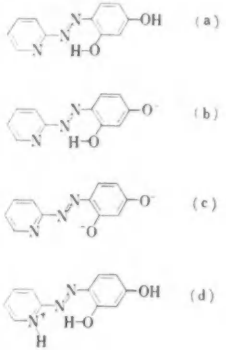



Fig. 2. Absorption spectra of benzeneazoresorcinol.
$7\times10^{-5}$ M: 1 cm. silica cell (Cary)
I: 8% ethanol
I': 95% ethanol
II: $4\times10^{-4}$ M borax in 8% ethanol
III: $3\times10^{-2}$ M NaOH in 8% ethanol
IV: 0.7 M NaOH in 8% ethanol




**Determination of Acid Dissociation Constants of PAR.**—From the pH dependency of the spectra the acid dissociation constants of PAR $k_{a_1}$ and $k_{a_2}$ defined by Eqs. 1 and 2 are estimated as about $10^{-6}$ and $10^{-12}$, respectively.

$$k_{a_1}=\frac{[C_{11}H_8O_2N_3^-]\,[H^+]}{[C_{11}H_9O_2N_3]} \quad (1)$$

$$k_{a_2}=\frac{[C_{11}H_7O_2N_3^{2-}]\,[H^+]}{[C_{11}H_8O_2N_3^-]} \quad (2)$$

In order to obtain more accurate values 100 ml. of $4.72\times10^{-5}$ M PAR solution was titrated with $1.085\times10^{-2}$ M potassium hydroxide solution at 25°C (Fig. 3). One proton caused by the first dissociation was neutralized and $k_{a_1}$ was calculated as $1.48\times10^{-6}$ ($pk_{a_1}=-\log k_{a_1}=5.83$) according to the following equation:

7a) T. Iwamoto, *Japan Analyst* (*Bunseki Kagaku*), **10**, 189 (1961).

8) M. T. Rogers, T. W. Campbell, R. W. Maatmann, *J. Am. Chem. Soc.*, **73**, 5122 (1951).

9) The absorption spectrum of 4-benzeneazoresorcinol in an ethanolic solution taken from the late Dr. F. Iimura's unpublished results shows also a singlet maximum at 375 mμ. The splitting may be elucidated in terms of solvent effect.

$$k_{a_1} = \frac{[H^+]\,(aC + [H^+] - [OH^-])}{C - (aC + [H^+] - [OH^-])} \qquad (3)$$

where $C$ stands for the total concentration of PAR and $a$ moles of base added per mole of the acid. Another proton caused by the second dissociation was not liberated under these conditions because of the low value of the second dissociation constant $k_{a_2}$, as foreseen by the absorption spectra measurements. Then it was approximately determined from absorption measurements of aqueous PAR solutions in the range of pH between 10 and 13.8 with a filter electrophotometer using the filters transparent in the vicinity of 420 and 485 mμ. From the curves in Fig. 4, $pk_{a_2}$ was estimated as 12.5 ($k_{a_2} = 3.2 \times 10^{-13}$).

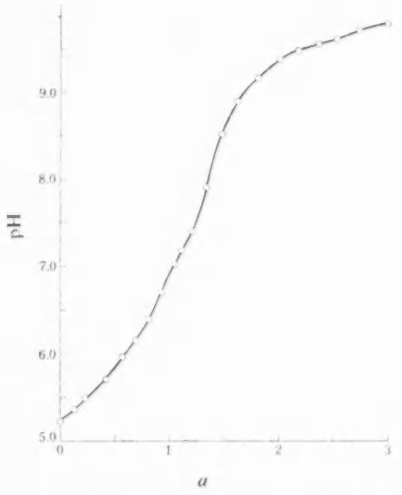



Fig. 3. pH-Titration of PAR free acid.
100 ml. of $5 \times 10^{-5}$ M PAR solution with 0.01 N KOH solution.
$a$: moles of base added per mole of acid

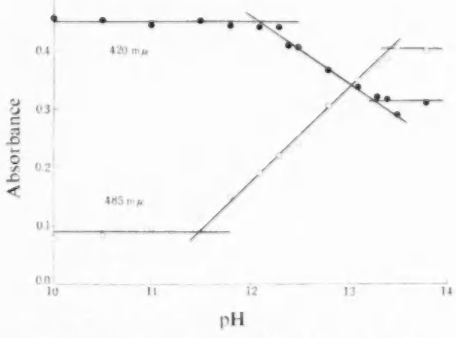



Fig. 4. Absorbance vs. pH of PAR solutions.
$5 \times 10^{-6}$ M PAR, 2 cm glass cell.
Full circle, at 420 mμ; open circle, at 485 mμ

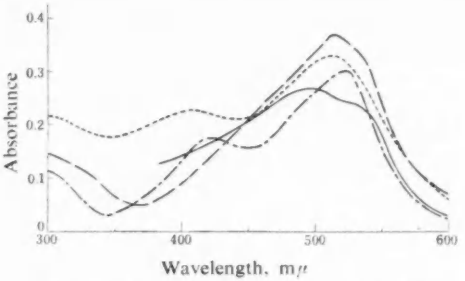



Fig. 5. Absorption spectra of metal-PAR chelates.
—— $Fe(PAR)_2$: $0.6 \times 10^{-5}$ M pH 4
—— $Co(PAR)_2$: $0.8 \times 10^{-5}$ M pH 4
—·— Cu(PAR): $1.0 \times 10^{-5}$ M pH 4
---- Pb(PAR): $1.0 \times 10^{-5}$ M pH 10
1 cm. silica cell (Shimadzu)

TABLE I. COMPOSITIONS AND MOLAR EXTINCTION COEFFICIENTS OF METAL-PAR CHELATES

| Metal | Composition | pH | ε at 517 mμ |
|---|---|---|---|
| Fe(III) | 1 : 2 | 4.0 | $4.2 \times 10^4$ |
| Co(II) | 1 : 2 | 4.0 | $4.2 \times 10^4$ |
| Ni(II) | 1 : 2 | 4.0 | $2.2 \times 10^4$ |
| Cu(II) | 1 : 1 | 4.0 | $3.0 \times 10^4$ |
| | 1 : 1 | 10.0 | $3.2 \times 10^4$ |
| Zn(II) | 1 : 1 | 10.0 | — |
| Cd(II) | 1 : 1 | 10.0 | — |
| Hg(II) | 1 : 1 | 10.0 | — |
| Pb(II) | 1 : 1 | 10.0 | $3.8 \times 10^4$ |

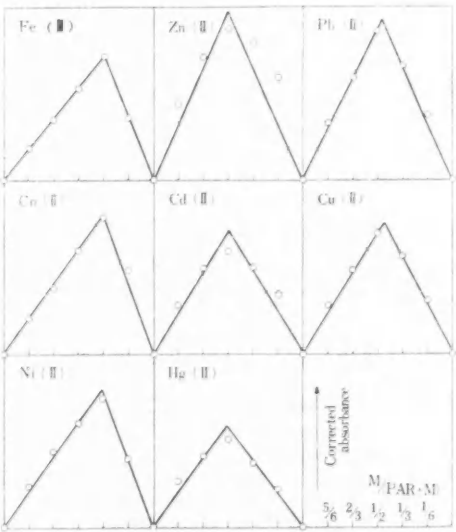
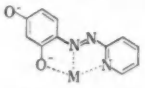



Fig. 6. Graphical determination of the composition of metal-PAR chelates.

**Compositions of PAR Chelates of Fe(III), Co(II), Ni(II), Cu(II), Zn(II), Cd(II), Hg(II) and Pb(II).**—Wehber[1] and Pollard et al.[3] reported the coloration of the chelates of PAR with various kinds of metals in aqueous solutions. In Fig. 5 are shown a few examples of absorption spectra measured by the present author. The composition of these chelates in aqueous solutions was determined by means of the continuous variation method using the filter photometer with a 517 mμ filter. The results and the molar extinction coefficients of the chelates are given in Table I. In Fig. 6, data are shown graphically. From these data PAR may be considered to act as terdentate ligand having three donor atoms in a plane[10]:



The details of the structure of metal-PAR chelare are now under investigation.

**Stability Constant of Copper(II)-PAR Chelate.**—In the presence of copper(II)-EDTA chelate, PAR may be applied as a metal indicator to the titration of metal cations which neither form colored chelates with PAR nor react with PAR rapidly and reversibly. To compare the function of the Cu-PAR indicator system with that of Cu-PAN[11], the stability constant of copper(II)-PAR chelate was determined by pH-titration. One hundred ml. of solution containing $4.72\times10^{-6}$ mol. of PAR and the equimolar amount of copper nitrate was titrated with the above-mentioned potassium hydroxide solution. The titration curve shown in Fig. 7 exhibits a marked inflection at $a\simeq2$. Acid dissociation and chelate formation of PAR are as follows:

$$H_2D = H^+ + HD^- \qquad (pk_{a_1}=5.83) \tag{4}$$

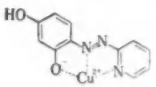
$$HD^- = H^+ + D^{2-} \qquad (pk_{a_2}=12.5) \tag{5}$$

$$Cu^{2+} + D^{2-} = CuD^{12)} \tag{6}$$

$$Cu^{2+} + H_2D = 2H^+ + CuD \tag{6'}$$

$$CuD + H^+ = HCuD^+ \tag{7}$$

where $H_2D$ is PAR in undissociated form, $HD^-$ in b form (p. 607) and $HCuD^+$ is one-protonated form of Cu-PAR chelate that may exist in considerably low pH region:



The equilibrium constant for Eq. 6, $k=[CuD]/[Cu^{2+}][D^{2-}]$, gives the stability constant of copper(II)-PAR chelate provided that the activity coefficient of each species is maintained constant. If $k_a'=[H^+][CuD]/[HCuD^+]$ is postulated as the acid dissociation constant for the process reverse to Eq. 7, Eq. 8 gives the relation between $k$, $k_{a_1}$, $k_{a_2}$ and the concentration of $D^{2-}$ throughout the titration under the experimental conditions:

$$k[D^{2-}]^2([H^+]^2/k_{a_1}k_{a_2}+[H^+]/k_{a_2}) - [D^{2-}][H^+]^2/k_{a_1}k_{a_2} = (a-1)+[H^+]-[OH^-] \tag{8}$$

where $C$ stands for the total concentration of PAR (=that of $Cu^{2+}$) and $a$ the moles of base added per mole of PAR.

With the assumption that at adjacent plots of the measurements in the buffer region of the titration curve the value of $[D^{2-}]$ is the same, $k$ was calculated to be $5\times10^{11}$ as the mean value from thirty sets of simultaneous equations derived from Eq. 8. $k_a'$, which can be considered as the second dissociation constant of a hypothetical dibasic acid $H_2CuD^{2+}$,

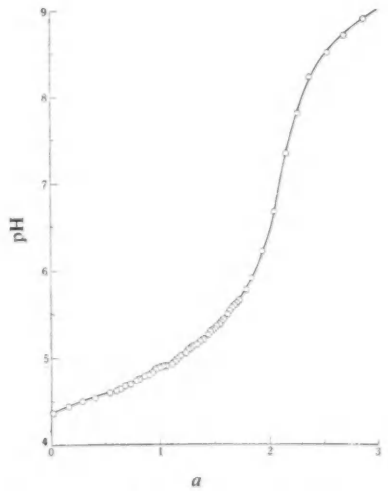



Fig. 7. Titration curve of copper(II)-PAR chelate.
$5\times10^{-5}$ M Cu-PAR solution 100 ml. with 0.01 M KOH solution
$\mu=0.1$ M $KNO_3$, 25°C
$a$: moles of base added per mole of chelate

10) Y. Muto, This Bulletin, **31**, 1017 (1958); F. Lions and K. V. Martin, *J. Am. Chem. Soc.*, **79**, 2733 (1957); F. Lions and H. A. Goodwin, ibid., **81**, 6415 (1959).

11) H. Flaschka and H. Abdine, *Z. anal. Chem.*, **152**, 77 (1956); *Chemist-Analyst*, **45**, 2 (1956).

12) It is not necessary for CuD to be neutral in charge, for PAR is considered as a terdentate ligand and the coordination requirement of copper(II) atom will be fulfilled by another unidentate anion (e. g. nitrate ion) in the solution.

was determined graphically[13] to be $5\times10^{-6}$ from the titration data.

### Analytical Aspects of PAR

**Cu-PAR Indicator in EDTA-Titrations.**—Pease and Williams[2] have determined the stability constant of copper(II)-PAN chelate to be approximately $10^{16}$. This value is considerably greater than that of PAR chelate, $5\times10^{11}$. Comparing the value for PAN chelate with that for copper(II)-EDTA chelate, $2\times10^{18}$, they have concluded "this is one reason that the copper(II)-PAN indicator may be successfully used in complexometric titrations of metals with EDTA".

According to Flaschka-Khalafallah's error-equation in visual end-point determination in chelatometric titration, Eq. 9[14], however, it may be concluded that $\Delta p$, the deviation of end-point (metal-combined indicator/free indicator=1/9) from equivalence-point, for the above-mentioned copper(II)-EDTA-PAN system is to be +0.04, i.e., the theoretical error is +4% when $C_M$ and $C_I$ were put as $10^{-3}$ and $10^{-6}$, respectively.

$$\Delta p=(9rC_M-0.01C_I-1/9k)/C_M \qquad (9)$$

where $C_M$: total concentration of metal,
$C_I$: total concentration of indicator,
$k$: stability constant of metal-indicator complex,
$K$: stability constant of metal-complexan, and $r=k/K$.

The error obtained here is contrary to Cheng's observation[15]. To make the error below 0.5%, the stability constant of metal-indicator complex must be below $10^{15}$. The value for Cu-PAR satisfies such a requirement. In regards to the relationship of the stability of copper(II)-indicator to that of copper(II)-EDTA, it may be concluded that PAR is a more accurate indicator than PAN provided that the stability constant of Cu-PAN is reliable. Nevertheless, for the practical applications as a titration indicator no remarkable difference between them, except the higher solubility of PAR in water, has yet been found out.

**PAR as a Detection Reagent for Heavy Metals.**—It must be mentioned that the high absorbancy in the visible region and the water-solubility of PAR chelates favor the detection of heavy metals and very high sensitivity can be achieved. For example, the identification limit of copper(II) in ordinary spot test was found to be 0.01 $\mu$g in 0.04 ml. test solution, i.e., limit of dilution is $1:2.5\times10^{-7}$, and that in resin spot test using a few grains of cation-exchange resin Dowex 50W-X8 in H-form as a collector of copper(II)-PAR chelate to be 0.0005 $\mu$g ($1:1.3\times10^{-8}$)[16].

### Summary

Acid dissociation stages of analytical reagent 4-(2-pyridylazo)-resorcinol (PAR) and metal chelate formation of PAR were investigated by absorption measurements and pH-titrations. The first acid dissociation constant was determined as $1.48\times10^{-6}$ ($pk_{a_1}=5.83$) and the second as $3.2\times10^{-13}$ ($pk_{a_2}=12.5$) at 25°C. PAR forms 1:2 chelate with Fe(III), Co(II) and Ni(II), and forms 1:1 chelate with Cu(II), Zn(II), Cd(II), Hg(II) and Pb(II). The stability constant of copper(II)-PAR chelate was determined as $5\times10^{11}$ at 25°C. Some analytical aspects of PAR were also discussed.

The author wishes to thank Dr. Eiiti Minami, Professor Emeritus, for his interst in this work and Mr. Kunihiko Mizumachi, Lecturer in Rikkio University, for his ardent encouragement and advice in the calculation of the chelate stability constant. He also thanks Dojin Pharmaceutical Laboratories for the gift of the sample of PAR.

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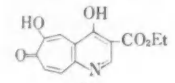
13) S. Glasstone, "An Introduction to Electrochemistry", Van Nostrand Co., New York (1956), p. 401.
14) H. Flaschka and S. Khalafallah, *Z. anal. Chem.*, **156**, 401 (1957).
15) K. L. Cheng, *Anal. Chem.*, **30**, 243 (1958).
16) M. Fujimoto and T. Iwamoto, unpublished results to be reported in detail together with the data for PAN.

# *A Ring-Chain Tautomerism in the Reaction Products of 3-Aminotropolone and Some Ethoxymethyleneacetates*[1]

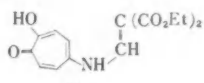
By Tetsuo Nozoe, Kozo Doi* and Kazuo Kitahara**

(Received April 11, 1960)

Slack and Attridge[2] reported the synthesis of a pyridotropolone (I) by application of the Gould-Jacobs' quinoline synthetic method[3] involving a process of pyrolysis of 5-(β, β-diethoxycarbonylvinylamino)tropolone (II), a condensation product of 5-aminotropolone and ethyl ethoxymethylenemalonate. This kind of synthetic method of pyridotropolones has also been applied to the other 5-aminotropolone derivatives[4] and 4-aminotropolone[5].



I



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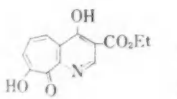
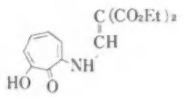


III

IV



V

In the present series of experiment an attempt was made to prepare a pyridotropolone (III) by application of the similar synthetic method to 3-aminotropolone (IV). Although this objective was not accomplished unfortunately, other interesting observations were made, which are described in this paper.

When 3-aminotropolone (IV) and ethyl ethoxymethylenemalonate were heated, a yellow condensation product of m.p. 138°C was formed in a good yield. Its analytical data agreed with those calculated for the anticipated diethoxycarbonylvinylaminotropolone (V). The ultraviolet absorption spectrum (Fig. 1) of the condensation product seemed to be fairly reasonable for the expected structure V, if the tropolone nucleus and the α, β-unsaturated ester system were to interact through the intermediate nitrogen atom.

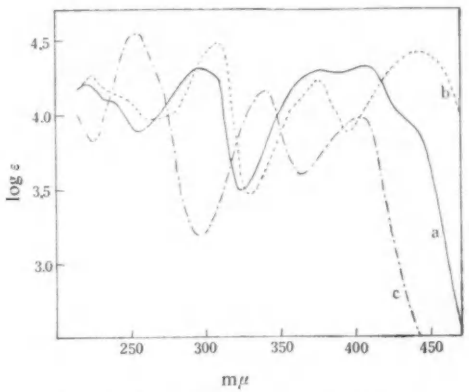



Fig. 1. Ultraviolet absorption spectra.
a) VIII in methanol
b) VIII in 0.01 N sodium hydroxide
c) IV in methanol

However, it has been found that pyrolysis of the above condensation product resulted in formation of not the anticipated pyridotropolone (III) but of another curious substances. Thus, on being heated at 250°C without a solvent, the condensation product afforded oxazolo[5 : 4-b]tropone* (VI) and ethyl malonate. The structure of the former VI was supported from its analytical values, determination of the molecular weight, and the close resemblance of its ultraviolet absorption curve (Fig. 2) to that of the known 2-methyloxazolo [5 : 4-b]-tropone[6] (VII). Ethyl malonate was identified as its dianilide[7].

The foregoing finding makes doubtful the assumption that the condensation product of the aminotropolone and ethoxymethylene-malonate may possess a structure like V. Virtually, the condensation product did not show any coloration with alcoholic ferric chloride and was inert to the action of diazomethane, the facts of which do not give

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1) This work in part was presented at the Local Meeting of the Chemical Society of Japan, Yonezawa, June, 1956.
2) R. Slack and C. F. Attridge, *Chem. & Ind.*, **1952**, 471.
3) R. G. Gould and W. A. Jacobs, *J. Am. Chem. Soc.*, **61**, 2890 (1939).
4) K. Yamane, *J. Chem. Soc. Japan, Pure Chem. Sec. (Nippon Kagaku Zasshi)*, **80**, 75 (1959).
5) K. Doi, *Bull. Chem. Research Inst. Non-Aqueous Solns., Tohoku Univ.*, **9**, 19 (1959).
6) Y. Kitahara, *Science Repts. Tohoku Univ., Ser. I*, **40**, 83 (1956).
* Very recently the same authors have reported the another syntheses and some reactions of the oxazolotropone (VI). [This Bulletin, **34**, 312 (1961)].
7) M. Freund, *Ber.*, **17**, 134 (1884).

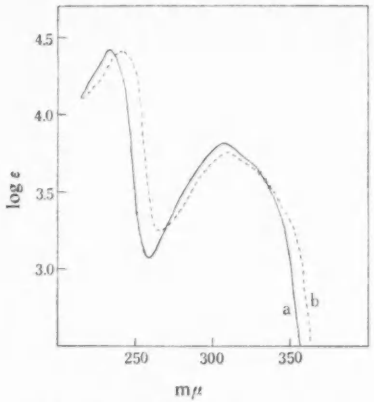
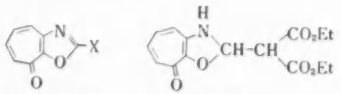



Fig. 2. Ultraviolet absorption spectra.
a) VI in methanol
b) VII in methanol

enough explanation for the condensation product to be a diethoxycarbonylvinylaminotropolone (V).

From the above facts it seems more reasonable to consider that the condensation product has a dihydro-oxazolotropone structure VIII.



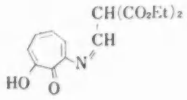

VI : X=H
VII : X=$CH_3$

VIII

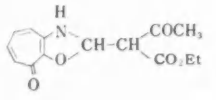
The ultraviolet absorption spectrum of VIII in an alkaline solution shows a red-shift in comparison to that in neutral solution, and this suggests that VIII results in ring-opening to V or IX in an alkaline solution (Fig. 1).

With aid to isolate the chain-isomer V or IX, the condensation product VIII was treated with ethanolic potassium hydroxide, neutralized carefully with dilute mineral acid, and subsequently extracted with chloroform. The fresh extract showed clearly a red coloration with ferric chloride, but the vacuum evaporation of the solvent resulted not in formation of the expected chain-isomer but in recovering of the raw material.

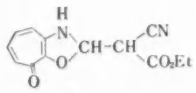
In the condensation reaction of 3-aminotropolone and ethoxymethylenemalonate, it is considered that the anticipated diethoxycarbonylvinylaminotropolone (V) or its isomeric azomethine derivative IX produces at first and spontaneously isomerizes to the ring-isomer VIII. It seems to leave no room for doubt, at any rate, that the condensation product of the aminotropolone and ethoxymethylenemalonate exists in the ring-form of VIII in a neutral state and that it exists in the chain-form of V or IX in an alkaline medium. That the ultraviolet absorption of VIII in methanol solution has maxima in the comparatively longer wavelength regions indicates probably, though not any evidences have been obtained, that VIII is ring-opening to V or IX at least in the condition of the spectral measurement.




IX




X




XI

On being heated with ethyl ethoxymethyleneacetoacetate and ethoxymethylenecyanoacetate in place of ethoxymethylenemalonate, 3-aminotropolone (IV) gave readily a condensation product, 2-(ω-acetyl-ω-ethoxy-carbonylmethyl)-2, 3-dihydroöxazolo[5 : 4-b]-tropone[8] (X) and 2-(ω-ethoxycarbonyl-ω-cyanomethyl)-2, 3-dihydroöxazolo[5 : 4-b]tropone (XI), respectively. The structures of these compounds were reasonably supported by the similarities of their ultraviolet absorptions (Fig. 3) to that of VIII and by the formation of the oxazolotropone (VI) by their pyrolysis.

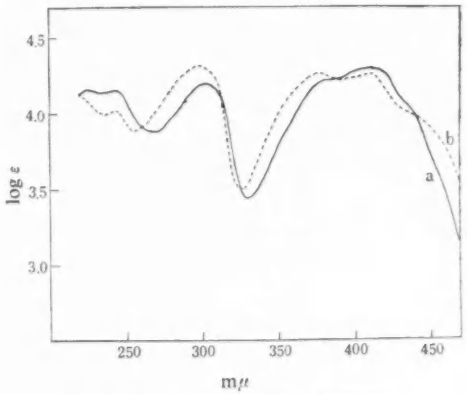



Fig. 3. Ultraviolet absorption spectra.
a) X in methanol
b) XI in methanol

The authors have found that the condensation products of *o*-aminophenol and the above three ethoxymethyleneacetates are also of the

8) Since the description of this work was completed, K. Yamane, *J. Chem. Soc. Japan, Pure Chem. Sec.* (*Nippon Kagaku Zasshi*), **81**, 509 (1960), have reported the synthesis of X by the same sequence.

cyclic structures of the corresponding benzoxazolines, the results of which will be described in the following paper.

## Experimental

The ultraviolet absorptions were determined in methanol solution, unless otherwise stated, with a Beckman model DU spectrophotometer.

**2-(ω, ω-Diethoxycarbonylmethyl)-2, 3-dihydrooxazolo[5:4-b]tropone (VIII).** — A mixture of 3-aminotropolone (IV, 1.0 g.) and ethyl ethoxymethylenemalonate (1.7 g.) was heated on an oil bath at 130°C for 30 min. After being cooled at room temperature, the residual solid was recrystallized from ethanol to give the dihydroöxazolotropone (VIII) as yellow leaflets, m. p. 138°C, in nearly quantitative yield.

Found: C, 58.60; H, 5.67; N, 5.05. Calcd. for $C_{15}H_{17}O_6N$: C, 58.63; H, 5.58; N, 4.56%. $\lambda_{max}$ mμ (log ε): in methanol, 220 (4.33), 295 (4.44), 381 (4.45), 408 (4.45); in 0.01 N sodium hydroxide, 225 (4.34), 310 (4.56), 377 (4.31), 442 (4.49).

The condensation product VIII did not show any coloration with alcoholic ferric chloride and remained inert to the action of diazomethane.

A mixture of VIII (0.3 g.), methanol (10 ml.), sodium hydroxide (0.4 g.) and water (5 ml.) was heated on a water bath at 50°C for 30 min. The orange solution so formed was cooled, neutralized cautiously with dilute hydrochloric acid, and then extracted with chloroform. The extract showed red coloration with ferric chloride, but its evaporation of the solvent under reduced pressure left only starting material VIII.

**Oxazolo[5:4-b]tropone (VI).**—VIII (1.45 g.) was placed in a Claisen flask of small capacity and heated on an oil bath at 230°C for 30 min. Colorless liquid (0.1 g.), which distilled out at 197~199°C and smelled like ethyl malonate, was collected. On being heated at 150°C with excess of aniline, it gave malonic dianilide, m. p. 275°C, undepressed on admixture with an authentic specimen[7]. The distilled residue, after extraction with warm benzene and subsequent evaporation of the solvent, crystallized from cyclohexane to give oxazolotropone (VI, 0.6 g.) as pale yellow prisms, m. p. 151~152°C.

Found: C, 65.60; H, 3.90; N, 9.40; mol. wt. (Rast), 146. Calcd. for $C_9H_5O_2N$: C, 65.30; H, 3.43; N, 9.52%; mol. wt., 147. $\lambda_{max}^{MeOH}$ mμ (log ε): 235 (4.42), 305 (3.80).

**2-(ω-Acetyl-ω-ethoxycarbonylmethyl)-2,3-dihydrooxazolo[5:4-b]tropone (X).** — A mixture of the aminotropolone (0.7 g.) and ethyl ethoxymethyleneacetoacetate[9] (0.9 g.) was heated at 130°C for 30 min. and the residual solid was crystallized from ethanol to give dihydroöxazolotropone (X) as yellow prisms, m. p. 136°C, in a nearly quantitative yield.

Found: C, 60.69; H, 5.42; N, 5.34. Calcd. for $C_{13}H_{13}O_5N$: C, 60.64; H, 5.45; N, 5.05%. $\lambda_{max}^{MeOH}$ mμ (log ε): 245 (4.30), 303 (4.35), 415 (4.45).

Pyrolysis of the product (X, 0.54 g.) at 250°C for 30 min. afforded the oxazolotropone (VI, 0.15 g.) and ethyl acetoacetate (50 mg.), identified as its anilide[10].

**2-(ω-Ethoxycarbonyl-ω-cyanomethyl)-2,3-dihydrooxazolo[5:4-b]tropone (XI).** — A mixture of the aminotropolone (140 mg.) and ethyl ethoxymethylenecyanoacetate[11] (170 mg.) was heated at 130°C for 30 min. and the residual solid was crystallized from methanol to give the condensation product (XI) as yellow needles, m. p. 182°C, in nearly quantitative yield.

Found: C, 60.06; H, 4.87; N, 10.86. Calcd. for $C_{13}H_{12}O_4N_2$: C, 59.99; H, 4.64; N, 10.77%. $\lambda_{max}^{MeOH}$ mμ (log ε): 245 (4.11), 300 (4.41), 378 (4.35), 410 (4.35).

Pyrolysis of XI (0.54 g.) as above described afforded also the oxazolotropone (VI, 0.2 g.) and ethyl cyanoacetate (50 mg.), identified as its amide[12].

The authors express their gratitude to Messrs. S. Ohyama, K. Kato, A. Iwanaga and S. Azumi for microanalyses.

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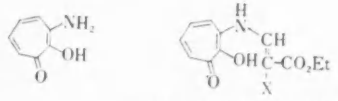
9) L. Claisen, *Ann.*, **297**, 16 (1897).
10) L. Knorr, ibid., **236**, 75 (1886).
11) M. E. G. deBollemont, *Bull. soc. chim. France*, [3] 25, 20 (1901).
12) B. B. Corson, R. W. Scott and C. E. Vose, "Organic Syntheses," Coll. Vol. I, 173 (1932).

# *A Note on the Ring-Chain Tautomerism in the Reaction Products of o-Aminophenol and Some Ethoxymethyleneacetates*

By Tetsuo Nozoe and Kozo Doi*

(Received August 25, 1960)

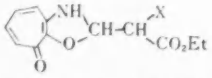
In the preceding paper[1], it was shown that the condensation reaction of 3-aminotropolone (I) and ethyl ethoxymethylenemalonate or some ethoxymethyleneacetates afforded, not the anticipated vinylaminotropolone (II), but its ring-tautomer, dihydro-oxazolotropone (III). This conclusion was drawn from the facts that the above condensation products did not show any coloration with ferric chloride test and were inert to the action of diazomethane, and that their pyrolyses resulted in a fragmentation to oxazolo[5:4-b]tropone (IV) and respective acetic acid derivatives. The authors stated, moreover, that the condensation products III probably exist in the chain-forms of II (or their possible azomethine type of isomers) in an alkaline medium.



I



(X=$CO_2Et$, CN, $COCH_3$)
II



(X=$CO_2Et$, CN, $COCH_3$)
III

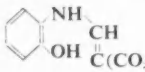
IV

There are not many systematic studies on the ring-chain tautomerism involving a nitrogen atom. Holly and Cope[2] elucidated this problem in the condensation products of *o*-aminobenzyl alcohol or *o*-hydroxybenzylamine with aldehydes or ketones through ultraviolet spectra and molecular refractions. Witkop and Beiler[3] also discussed this tautomerism in the arylidene Schiff bases derived from *o*-aminobenzyl alcohol through the spectral measurements.

From the above point of view, the present authors have felt interest in a possible ring-chain tautomerism between the condensation products of *o*-aminophenol, analogous to 3-aminotropolone (I), and ethoxymethyleneacetates. In this series of experiments, the authors have obtained information similar to that in the case of the aminotropolone; these will be described below in brief.

Condensations of anilines and ethoxymethyleneacetates have been often carried out for many syntheses of quinolines[4] and for identifications of anilines[5], but no report seems to have been made on the condensation of *o*-aminophenol and ethoxymethyleneacetates.

On being heated with ethyl ethoxymethylenemalonate, *o*-aminophenol afforded a condensation product of colorless crystals, m. p. 140~141°C, in a good yield. It did not show any coloration with alcoholic ferric chloride and was inert to the action of diazomethane. As might have been expected from the conclusions in the case of 3-aminotropolone (I), the above experimental results show that the condensation product is not the anticipated vinylaminophenol (V) or its possible isomer of the Schiff base type but is presumably 2-($\omega$, $\omega$-diethoxycarbonylmethyl)benzoxazoline (VI). The reaction product, moreover, resulted in fission to form benzoxazole and ethyl malonate on pyrolysis, and this fact probably affords a more powerful proof for the assignment of structure VI to the condensation product.



V

VI: X=$CO_2Et$
VII: X=$COCH_3$
VIII: X=CN

The ultraviolet absorption of the compound VI in an alkaline solution has maxima at longer wavelength region than in a neutral solution (Fig. 1). This fact indicates probably that the compound VI may exist in the chain-form of V (or its isomeric Schiff base) in an alkaline medium, the conclusion of which is analogous to that of the case in the condensation products of 3-aminotropolone[1].

The use of ethoxymethyleneacetoacetate and ethoxymethylenecyanoacetate, in place of

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1) T. Nozoe, K. Doi and K. Kitahara, This Bulletin, **34**, 611 (1961).

2) F. W. Holly and A. C. Cope, *J. Am. Chem. Soc.*, **66**, 1875 (1944).

3) B. Witkop and T. W. Beiler, ibid., **76**, 5589 (1954).

4) R. H. Reitsma, *Chem. Revs.*, **43**, 43 (1948).

5) G. R. Lappin, *J. Chem. Educ.* **28**, 126 (1951).

ethoxymethylenemalonate, in this condensation reaction afforded the respective benzoxazoline VII and VIII in a good yield. These structures were presumed from the facts that their ultraviolet absorptions were similar to that of the compound VI and that their pyrolyses yielded benzoxazole.

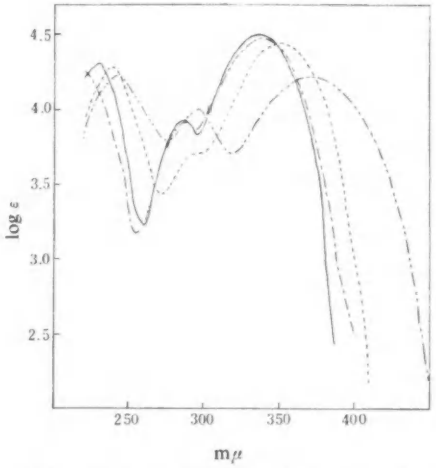


Fig. 1. Ultraviolet absorption spectra in methanol: curve —— VI; curve ---- VII; curve ——— VIII; curve ——— VI in 0.1 N sodium hydroxide solution.

## Experimental

The ultraviolet absorptions were measured in methanol, unless otherwise stated, with a Beckman model DU spectrophotometer.

**2-(ω, ω-Diethoxycarbonylmethyl)benzoxazoline (VI).**—A mixture of *o*-aminophenol (1.1 g.) and ethyl ethoxymethylenemalonate (2.2 g.) was heated on an oil bath at 130°C for 30 min., and then the residual solid was recrystallized from ethanol to form the benzoxazoline VI as colorless prisms, m. p. 140~141°C, in a nearly quantitative yield.

Found: C, 60.11; H, 5.72; N, 5.04. Calcd. for $C_{14}H_{17}O_5N$: C, 60.20; H, 6.14; N, 5.02%.

$\lambda_{max}$ mμ (log ε): in methanol, 230 (4.30), 286 (3.92), 335 (4.49); in 0.1 N sodium hydroxide, 243 (4.23), 295 (4.00), 370 (4.23).

**Pyrolysis of the Compound VI.**—The above benzoxazoline VI (5.6 g.) was placed in a Claisen flask with a small capacity and heated on an oil bath at 250°C. Vigorous boiling occurred and colorless liquid distilled out, which was separated into the two fractions by their boiling points at ordinary pressure: a) b. p. 175~185°C, 1.6 g., and b) b. p. 195~199°C, 2.7 g. Fraction (a) was distilled once again and the portion boiled at 180~182°C was collected. The cooled distillate crystallized to give benzoxazole (0.97 g.), alone and mixed m. p. 30~31°C[6]. The fraction (b), with an odor like that of ethyl malonate, afforded malonic dianilide, alone and mixed m. p. 275°C[7], on being heated with excess of aniline at 150°C.

**2-(ω-Acetyl-ω-ethoxycarbonylmethyl)benzoxazoline (VII).**—A mixture of *o*-aminophenol (1.1 g.) and ethyl ethoxymethyleneacetoacetate (1.9 g.) was heated at 130°C for 20 min. and the residual solid was recrystallized from methanol to give the benzoxazoline (VII) as colorless prisms, m. p. 146~147°C, in a good yield.

Found: C, 62.66; H, 5.98; N, 5.61. Calcd. for $C_{13}H_{15}O_4N$: C, 62.64; H, 6.07; N, 5.62%.

$\lambda_{max}^{MeOH}$ mμ (log ε): 238 (4.28), 350 (4.45).

VII resulted in the formation of benzoxazole and ethyl acetoacetate, identified as its anilide[8], on pyrolysis at 250°C.

**2-(ω-Ethoxycarbonyl-ω-cyanomethyl)benzoxazoline (VIII).**—An equimolar mixture of *o*-aminophenol and ethyl ethoxymethylenecyanoacetate was heated at 100°C for 30 min. and the residual solid crystallized from methanol to form the benzoxazoline (VIII) as colorless needles, m. p. 191~192°C, in a good yield.

Found: C, 62.04; H, 5.04; N, 11.90. Calcd. for $C_{12}H_{10}O_3N_2$: C, 62.06; H, 5.21; N, 12.06%.

$\lambda_{max}^{MeOH}$ mμ (log ε): 287 (3.91), 340 (4.47).

Pyrolysis of the compound VIII at 250°C gave also benzoxazole and ethyl cyanoacetate, identified as its amide[9].

The authors express their gratitude to Professor Yoshio Kitahara, the Chemical Research Institute of Non-Aqueous Solutions of Tohoku University, for his kind advice, to Mr. S. Ohyama and Miss Y. Endo for microanalyses.

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6) A. Ladenburg, *Ber.*, **10**, 1124 (1877).
7) M. Freund, ibid., **17**, 134 (1884).
8) L. Knorr, *Ann.*, **236**, 75 (1886).
9) B. B. Corson, R. W. Scott and C. E. Vose, "Organic Syntheses", Coll. Vol. I (1932), p. 173.

# *On the Structure of 2-Mercaptotropones*

By Tetsuo Nozoe and Kazuo Matsui

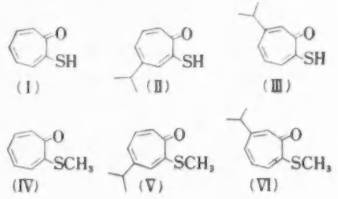
(Received August 16, 1960)

2-Mercaptotropone (I) was synthesized in 1953 by Nozoe and his collaborators[1,2]. It comes as reddish orange crystals of m. p. 55°C and the compound was assumed to be present in two tautomeric forms, A and B. Alkylation

(A) (B)

and acylation of I afford only sulfur-substituted derivatives, while reaction with hydrazine gives 2-hydrazinotropone. Bromine easily effects an oxidation to 2, 2′-ditroponyl disulfide. These facts suggest a structure A of this compound and this was named 2-mercaptotropone. But further examination on its physicochemical properties as well as those of its homologs suggested that this should rather be a 2-hydroxyl derivative of tropothione, structure B, and details of this work are described herein.

Physical measurements were carried out with 4-isopropyl-2-mercaptotropone (II), 6-isopropyl-2-mercaptotropone (III), 2-methylthiotropone (IV), 4-isopropyl-2-methylthiotropone (V), and 6-isopropyl-2-methylthiotropone (VI)[3], besides the 2-mercaptotropone (I).



**Ultraviolet Absorption Spectra**[4].—The ultraviolet absorption spectra of I, II and III are indicated in Fig. 1 and those of IV, V and VI in Fig. 2. As will be seen from these, the spectral curve of 2-mercaptotropones in Fig. 1 shows a fair shift to the longer wavelength side than that of 2-methylthiotropones in Fig. 2, indicating that there is an essential difference in the structure of these two kinds of compounds. This relationship is the same as

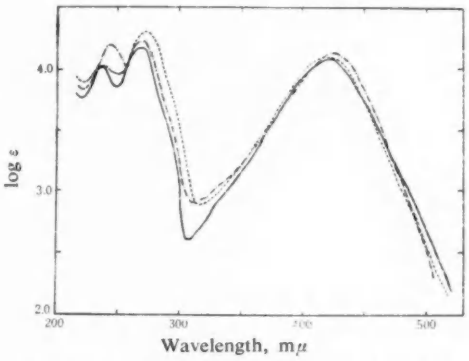



Fig. 1. Ultraviolet absorption spectra in cyclohexane.
——— I ------ II —·—· III

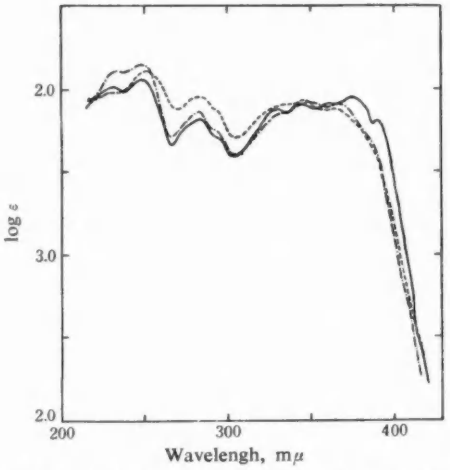



Fig. 2. Ultraviolet absorption spectra in cyclohexane.
——— IV ------ V —·—· VI

that between 2-thiopyridone and its *S*-methyl derivative[5], and if the B type of the structure is assigned to 2-mercaptotropones, the difference in ultraviolet absorptions could be explained as a bathochromic shift due to the C=S group.

1) T. Nozoe, M. Sato and K. Matsui, *Proc. Japan Acad.*, **29**, 22 (1953).
2) Idem, *Sci. Repts. Tohoku Univ., I*, **37**, 211 (1953).
3) K. Matsui, This Bulletin, **33**, 1448 (1960).
4) Measured by a Beckman Model DU spectrophotometer.
5) A. Albert and B. Barlin, "Current Trends in Heterocyclic Chemistry", Butterworths Scientific Publications, London (1958), p. 51.

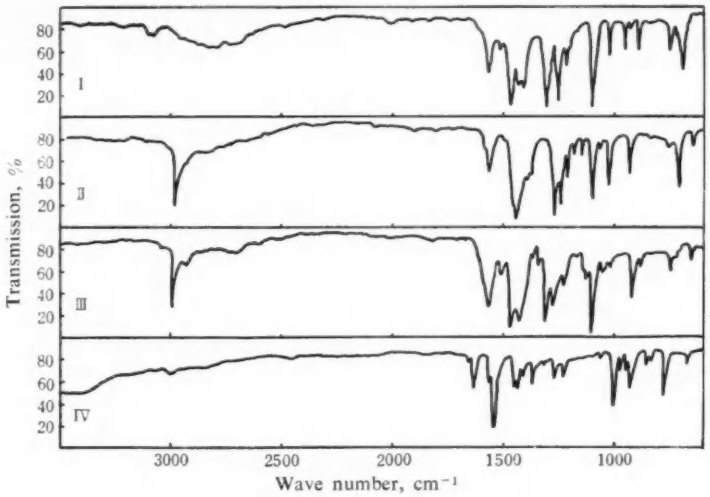



Fig. 3. Infrared absorption spectra.
I in 0.5% $CCl_4$ soln. II in 0.5% $CCl_4$ soln.
III in 0.5% $CCl_4$ soln. IV in KBr-pellet

**Infrared Absorption Spectra**[2,6]. — Infrared absorption spectra of I, II, III and IV are shown in Fig 3. The absoprtion of IV in the double-bond region is similar to those observed in tropone, 2-methoxytropone, and 2-halotropone[7], but the spectra of I, II and III are quite different from those seen in tropones and tropolones in general. Furthermore, examination of the spectra of I in the 3000 $cm^{-1}$ region indicates the presence of a broad and weak absorption in the region of 3000～2600 $cm^{-1}$. It is rather appropriate to consider that I takes the structure B and the $\nu_{OH}$ absorption has been shifted to lower wave-numbers by chelation, than a shift of $\nu_{SH}$ absorption to higher wave-numbers side from the usual absorption at 2600～2550 $cm^{-1}$.

The absence of a strong absorption assignable to the C=O group in a higher wave-numbers side than 1500 $cm^{-1}$ in the double-bond region also agrees with the structure B and considering Mecke's law[8] the absorption at 1100 $cm^{-1}$ is assumed to correspond to $\nu_{C=S}$.

The same thing may be said of II and III, and 2-mercaptotropones are therefore assumed to take the B of the type structure from infrared absorption spectral examinations.

**Nuclear Magnetic Resonance Spectra**[9]. — The NMR spectra of I, II, III and IV were measured in carbon tetrachloride solution at 40 Mc./sec. at room temperature, with cyclohexane as the internal reference. The results are indicated in Fig. 4. It should be noted here that in I, II and III, the resonance line of the ring proton appears as two signals, at 280 and 230 c. p. s. Since the ring proton appears as one signal at ca. 240 c. p. s. in tropone and tropolone[10], the small signal at 280 c. p. s. in the considerably lower magnetic field side should be assigned to the ring proton

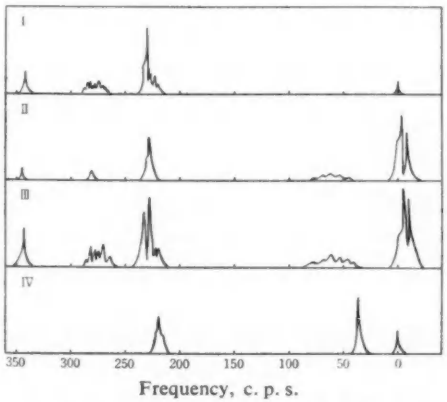



Fig. 4. NMR spectra of I, II, III and IV.

6) Measured by a Perkin-Elmer Model 21 double beam spectrophotometer.
7) S. Kinumaki, K. Aida and Y. Ikegami, *Sci. Repts. Reseach Inst. Tohoku Univ.*, A-8, 264 (1956).
8) R. Mecke, R. Mecke and A. Lüttringhaus, *Chem. Ber.*, 90, 975 (1957).
9) Measured by a Varian V 4300 B spectrometer.
10) D. Ginsberg, "Chemistry of Non-benzenoid Aromatic Compounds", Interscience Publishers, New York (1959), p. 380.

next to sulfur group. Further, the fact that this is absent in IV suggests that, I, II and III take the B type of the structure, and the signal of proton attached to the carbon next to the C=S group appears in the lower magnetic field side because is it in a different magnetic surrounding from other protons.

The resonance line at ca. 340 c. p. s. in I, II, and III may be assignable to SH group, but the OH line in tropolone appears at ca. 280 c. p. s.[10] This is in reverse of the general observation that the resonance line of SH compounds appears in a higher magnetic field than the corresponding OH compounds[11,12]. This fact also denies the A type of the structure.

**p$K_a$ value.**—The fact that p$K_a$ value of I (5.89)[13] is smaller than that of tropolone (6.92)[14], is in agreement with the general observation that thiophenols show smaller p$K_a$ value than the corresponding phenols. The difference of I and tropolone is, however, only 1 p$K_a$ unit, and this rather small difference compared with that, ca. 3 p$K_a$ unit[15,16], between thiophenols and phenols might be explained by the assignment of the structure B rather than A to I as follows.

2-Thiopyridones[17] show smaller p$K_a$ values than the corresponding 2-pyridones[18] by ca. 2 p$K_a$ unit, which is presumably due to the difference in inductive and mesomeric effect between the C=S and the C=O group. Similarly, it might be expected that in the case of I, structure B, and the tropolone, the C=S group in I should activate the OH group, more than the C=O group in tropolone does. But spacious and electron-rich sulfur atom induced by these electronic effects of the C=S group, conversely tend to control the liberation of proton in the OH group located close by*, more than does the oxygen atom in tropolone.

As a result of these opposing effects of the C=S group in I, the small p$K_a$ difference between I and tropolone is understandable without inconsistency.

**Solubility.** — Mercaptans in general are practically insoluble in water, but the solubility of I in water is 0.846 g./l.[13] Such a large degree of solubility also supports the structure B.

The results of the foregoing ultraviolet, infrared, and NMR spectral measurements, p$K_a$ value, and solubility, all indicate the appropriateness of the B type of the structure for 2-mercaptotropones. It has therefore been clarified that, although the compounds behave as A type of the structure during various reactions, they take the B type of the structure in a static state.

Consequently, the conventional structure A for 2-mercaptotropone (I) should be corrected and the structure B, i. e. 2-hydroxytropothione, is forwarded.

The authors are grateful to Tanabe Seiyaku Co., Ltd. for allowing one (Matsui) of the authors to take part in this research at Sendai. The authors' deepest gratitudes are expressed to Dr. T. Isobe and his colleagues, Chemical Institute of Non-Aqueous Solutions, Tohoku University, for their technical cooperation and keen discussion on NMR spectra, and to Mr. Y. Ikegami, the same Institute, for his helpful advices in infrared analyses.

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11) B. P. Dailey and J. N. Shoolery, *J. Am. Chem. Soc.*, **77**, 3977 (1955).
12) L. H. Meyer, A. Saika and H. S. Gutowsky, ibid., **75**, 4567 (1953).
13) N. Yui, *Sci. Repts. Tohoku Univ., I*, **40**, 114 (1956).
14) Idem., ibid., **40**, 50 (1956).
15) G. Schwarzenbach and H. Egli, *Helv. Chim. Acta*, **17**, 1176 (1934).
16) W. H. Fletcher, *J. Am. Chem. Soc.*, **75**, 3784 (1953).
17) R. A. Jones and A. R. Katritzky, *J. Chem. Soc.*, **1958**, 3610.
18) A. Albert and J. N. Phillips, ibid., **1956**, 1294.

* It should be noted here that tropone and tropolone derivatives with the SH group are extremely unstable and undergo dehydrogenative condensation to yield disulfides, unless the SH group is situated at the carbon next to the C=O group and a hydrogen bond between these groups is formed[2].

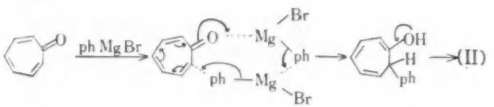
# *Reaction of Troponoids and Organometallic Compounds. VI*. Reaction of Tropone with Grignard Reagents***

By Tetsuo NOZOE, Toshio MUKAI and Takahiro TEZUKA

(Received August 29, 1960)

It has been known that tropolone methyl ethers undergo reaction with Grignard reagents to give tropone derivatives substituted in the 2-position[1,2]. Considering that tropone, the parent compound of tropolone, possesses some degree of ketonic properties[3], its Grignard reaction is considered to be of interest, but no report has been published on this subject. The present paper describes the reaction of methyl-, isopropyl- and phenylmagnesium halide on tropone and the preparation of tropone derivatives via the products thereby formed.

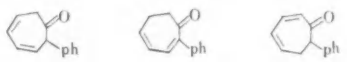
Applications of two molar equivalents of phenylmagnesium bromide on tropone (I) and subsequent decomposition of the magnesium complex with dilute hydrochloric acid gives an oil II, $C_{13}H_{12}O$; 2,4-dinitrophenylhydrazone, m. p. 135°C, maleic anhydride adduct, m. p. 147°C. Catalytic reduction of II results in absorption of 2 molar equivalents of hydrogen to form 2-phenylcycloheptanone. The NMR spectrum of II at 40 Mc. (Fig. 1)*** exhibits three sorts of signals due to phenyl (a), vinyl (b) and methylene (c) protons respectively. These observations indicate that II is one of the 2-phenylcycloheptadienone such as A, B or C, formed by ketonization of enolic intermediate III which was produced by 1, 8-addition of the Grignard reagent to the conjugated system in I.




(I) (III)

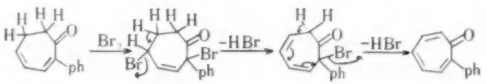
As in the reaction of Grignard reagents with tropolone methyl ethers, two molar equivalents of the reagent are also necessary in this reaction in order to obtain II in fair yield. This implies that the reaction proceeds through a complex formation between tropone and two molecules of the Grignard reagent, analogous to the cyclic intermediate suggested by Swain and others[4].

The infrared spectrum of II shows a carbonyl band at 1660 $cm^{-1}$ characteristic of the conjugated dienone system[5], implying that II is represented by B or C. The maxima in the ultraviolet spectrum of II, 235 and 315 m$\mu$ (log $\varepsilon$: 3.98 and 3.85), also supports this view, and moreover, the bathochromic shift of 23 and 13 m$\mu$ compared with cyclohepta-2, 4-dien-1-one[6], 292 m$\mu$ (log $\varepsilon$: 3.97) and eucarvone[7], 302 m$\mu$ (log $\varepsilon$: 3.82) respectively, indicates that II can be best represented by B rather than C.




(A) (B) (C)

II absorbs one molar equivalent of bromine in acetic acid to form an oily dibromide e. g. IV, which lacks the intensive maxima above 220 m$\mu$ in the ultraviolet spectrum. When IV is heated under reduced pressure, hydrogen bromide is liberated to form the hydrobromide of 2-phenyltropone, m. p. 145~147°C (30%), from which 2-phenyltropone (V)[1] is formed.




(II) (IV) (V)

Oxidation of II with selenium dioxide or chromium trioxide gives also 2-phenyltropone in 75 and 10% yield respectively.

In an earlier work[8] in this laboratory, it

* Part V: K. Kikuchi, This Bulletin 33, 628 (1960). This report is also Part VI of Tropones.

** Presented before the Local Meeting of the Chemical Society of Japan, Sendai, December, 1958.

1) (a) T. Nozoe, T. Mukai and J. Minegishi, *Proc. Japan Acad.*, **27**, 419 (1951); (b) T. Nozoe, T. Mukai and I. Murata, ibid., **28**, 142 (1952); (c) T. Nozoe, T. Mukai, J. Minegishi and T. Fujisawa, *Sci. Repts. Tohoku Univ., I*, **37**, 388 (1953).

2) (a) K. Kikuchi, *J. Chem. Soc. Japan, Pure Chem. Sec. (Nippon Kagaku Zasshi)*, **77**, 1439 (1956); (b) K. Kikuchi, ibid., **81**, 505 (1960); (c) K. Kikuchi, This Bulletin, **33**, 628 (1960).

3) T. Nozoe, T. Mukai and K. Takase, *Sci. Repts. Tohoku Univ., I*, **39**, 164 (1956).

*** All NMR spectra were measured with a Varian V-4300B spectrometer.

4) C. G. Swain and H. B. Boyles, *J. Am. Chem. Soc.*, **73**, 871 (1951).

5) Eucarvon shows carbonyl band at 1661 $cm^{-1}$.

6) E. E. van Tamelen and G. T. H. Hildahl, *J. Am. Chem. Soc.*, **75**, 5451 (1953).

7) E. J. Corey and H. J. Burke, ibid., **76**, 5257 (1954).

8) (a) T. Nozoe, T. Mukai, M. Ishii and Y. Ikegami, unpublished work; (b) T. Mukai, This Bulletin, **31**, 852 (1958).

had been shown that the reaction of phenylmagnesium bromide on 2-phenyltropone afforded colorless plates (VII) $C_{19}H_{16}O$, m. p. 87°C, accompanied by 2,7-diphenyltropone (VIII), both of which gave 2,7-diphenylcycloheptanone on catalytic hydrogenation, but the structure of compound VII remained unestablished. It is likely now that VII has the structure as shown below.

(VII) (VIII)

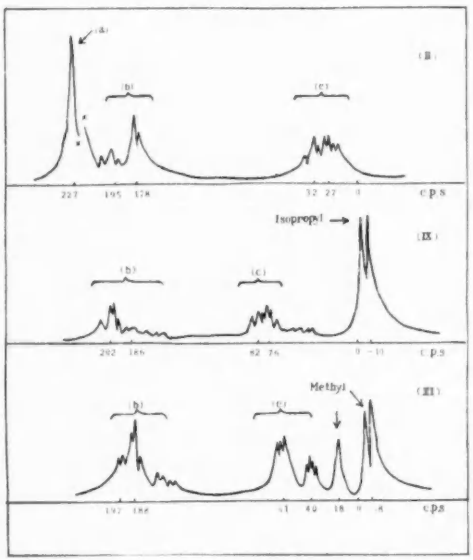
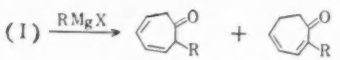



Fig. 1. NMR spectra of 2-phenyl-(II), 2-isopropyl-(IX) and 2-methylcyclohepta-dienone-(XI) at 40 Mc., relative to cyclohexane as inner reference.

The reaction of tropone with isopropylmagnesium bromide affords a liquid (IX), $C_{10}H_{14}O$, $\lambda_{max}$ 302 mμ (log ε: 3.31), which absorbs 2 molar equivalents of hydrogen on catalytic hydrogenation to give 2-isopropylcycloheptanone. The NMR spectrum of IX (Fig. 1) also suggests the cycloheptadienone type. Since the infrared spectrum indicates two carbonyl absorption bands at 1705 and 1658 $cm^{-1}$, it is assumed that IX is a mixture of IXa and IXb ($R=i\text{-}C_3H_7$). From the comparison of the absorption intensity in the ultraviolet spectrum of IX at 302 mμ with that of eucarvon (mentioned above), the proportion of IXa to IXb is assumed to be about 2 to 1.




(IXa) $R=i\text{-}C_3H_7$ (IXb) $R=i\text{-}C_3H_7$
(XIa) $R=CH_3$ (XIb) $R=CH_3$

IX adds one molar equivalent of bromine, but the dibromide thereby formed easily loses hydrogen bromide during removal of the solvent to afford an oily product (X) which gives the known 2-amino-7-isopyropyltropone[9] on being treated with hydrazine hydrate, indicating that X is 2-isopropyltropone.

Although the ultraviolet spectrum and the infrared diagram of X are analogous to those of known 2-methyl- and 2-ethyltropone[10], X does not form a picrate, an oxime or a 2,4-dinitrophenylhydrazone by the usual process and this may be due to the steric hindrance of the isopropyl group.

Similarly, the reaction of tropone with methylmagnesium iodide gives an oil (XI), $\lambda_{max}$ 235 and 298 mμ (log ε: 3.54 and 3.53), whose catalytic hydrogenation produces 2-methylcycloheptanone. Treatment of XI with bromine easily effects bromination-dehydrobromination to give the known 2-methyltropone.

The infrared spectrum of XI exhibits carbonyl bands at 1710 and 1665 $cm^{-1}$ as in the case of IX, and XI is considered to be a mixture of XIa and XIb ($R=CH_3$). This is also supported by its NMR spectrum (Fig. 1) in which two kinds of signals due to the methyl group appear at +18 c. p. s. (singlet) and −8 c. p. s. (doublet). The former is assumed to come from the methyl group in XIb, whereas the latter is due to the methyl group in XIa. Moreover, the calculation of the areas of two signals due to methyl groups in NMR spectrum and the intensity in the ultraviolet spectrum of XI shows that XIa is more prominent than XIb in that mixture.

Both IX and XI are easily dehydrogenated by the treatment with selenium dioxide to give 2-isopropyl- or 2-methyltropone in 55 and 60% yields, respectively.

It follows, therefore, that the Grignard reaction of tropone is also useful as a general method for the preparation of tropone derivatives.

After the present work had been completed, it was learned very recently that Closs and Closs[11] had obtained a compound XII ($R=H$ or $CH_3$) from the reaction of methyllithium on tropone or 2-methyltropone. They also

9) T. Nozoe et al., unpublished work.
10) T. Mukai, *J. Chem. Soc. Japan, Pure Chem. Sec.* (*Nippon Kagaku Zasshi*), **79**, 1547 (1958).
11) G. L. Closs and L. E. Closs, Abstracts of Papers, National Meeting of the American Chemical Society, Cleveland, April, 1960.

(XII)

obtained similar compounds by the application of methylene chloride and methyllithium on phenol or cresol, but details are not available. Our results in which the conjugated dienones with the double bond in position different from that in XII (R=H) has been obtained, would be due to a migration of the double bond during the decomposition of the magnesium complex with dilute hydrochloric acid.

## Experimental[12]

**2-Phenylcycloheptadienone (II).**—A solution of 3.0 g. of tropone in 40 ml. of absolute ether was added dropwise at 0°C with stirring to 2.2 mol. equiv. of Grignard reagent prepared from 10.3 g. of bromobenzene and 1.5 g. of magnesium in 40 ml. of absolute ether. After additional stirring for half an hour, the reaction mixture was decomposed with 1 N hydrochloric acid, extracted with ether, washed with water and dried over anhydrous sodium sulfate. Removal of the solvent afforded 7.5 g. of crude oil, whose distillation in vacuo gave 4.35 g. (84%) of pale yellow oil (II), b. p. 139～145°C (3 mmHg), $n_D^{15}$ 1.4890, $\lambda_{max}^{MeOH}$ 235 mμ (log ε: 3.98), 315 mμ (log ε: 3.85). For analysis, this oil was redistilled to give b. p. 143～145°C (3 mmHg).

Found: C, 84.31; H, 6.38. Calcd. for $C_{13}H_{12}O$: C, 84.75; H, 6.57%.

Application of 1.0 and 1.5 molar equivalents of the Grignard reagent on tropone afforded II in 30% and 75% yields with the recovery of tropone (35 and 3% respectively).

2,4-Dinitrophenylhydrazone, m. p. 134～135°C, $\lambda_{max}^{MeOH}$ 375 mμ (log ε: 4.15).

Found: C, 62.54; H, 4.31; N, 15.08. Calcd. for $C_{19}H_{16}O_2N_4$: C, 62.63; H, 4.43; N, 15.38%.

**Catalytic Reduction of 2-Phenylcycloheptadienone (II).**—A solution of 300 mg. of II in 4.5 ml. of ethanol was hydrogenated at 1 atm. and 18°C with prereduced palladium-carbon catalyst. After 125 min., 87 ml. (2.4 mol. equiv.) of hydrogen was absorbed. Removal of the catalyst and evaporation of the solvent afforded 300 mg. of an oil, which gave semicarbazone m. p. 150～151.5°C, undepressed on admixture with an authentic sample of 2-phenylcycloheptanone semicarbazone[13a].

**Bromination of 2-Phenylcycloheptadienone (II).**—A solution of bromine in acetic acid (88 mg./0.5 ml.) was added dropwise at 0°C to a solution of 100 mg. of II in 5 ml. of acetic acid, by which 1.2 mol. equiv. of bromine was absorbed. After stirring for one hour, the reaction mixture was diluted with water, extracted with benzene, washed with water and dried over anhydrous sodium sulfate. Removal of the solvent at room temperature under reduced pressure gave 200 mg. of brown oil, a chromatographic purification of which on alumina afforded dibromide IV as a viscous oil.

Found: C, 44.76; H, 3.34. Calcd. for $C_{13}H_{12}OBr_2$: C, 45.36; H, 3.51%.

**2-Phenyltropone.**—a) The dibromide (200 mg.) obtained above was heated at 80°C under reduced pressure (20 mmHg) overnight. The resultant residue was extracted with benzene, washed with water and dried. Evaporation of the solvent and chromatographic purification on alumina yielded 2-phenyltropone (70 mg.) as a reddish oil. On treatment of this oil (70 mg.) with hydrazine hydrate, crystals (20 mg.), m. p. 200～202°C were obtained. Recrystallization from benzene gave yellow needles, m. p. 203～204°C, identical with authentic 2-amino-7-phenyltropone[13].

b) II (1 g.) was brominated in acetic acid and the reaction mixture was treated as described above. On removal of the solvent at 80°C, 400 mg. of 2-phenyl tropone as colorless needles, m. p. 145～147°C*, which showed almost identical ultraviolet absorption maximum with that of 2-phenyltropone. This hydrobromide (200 mg.) was heated at 100°C under reduced pressure (20 mmHg) for 2 hr. and subsequently sublimed to afford 90 mg. of yellow needles, m. p. 82～83°C, undepressed on admixture with authentic 2-phenyltropone.

**Dehydrogenation of II with Selenium Dioxide.**—A solution of 200 mg. of II in 2 ml. of dioxane was heated under reflux with selenium dioxide (140 mg.) for 7 hr. The deposited selenium (30 mg.) was filtered off and the filtrate was concentrated. The resultant residue was dissolved in benzene, washed successively with saturated sodium bicarbonate solution and water, and dried. On removal of the solvent, 150 mg. (75%) of crystals, m. p. 70～75°C was obtained. Recrystallization from benzene and chromatographic purification on alumina gave yellow prisms, m. p. 83～84°C, identical with 2-phenyltropone.

**Oxidation of II with Chromium Trioxide.**—A solution of 1.9 g. of II in 6 ml. of pyridine was added to pyridine-chromic acid complex (1 g. $CrO_3$/10 ml. pyridine) at 15～20°C. After stirring for 10 hr. and standing for another 12 hr. at room temperature, the reaction mixture was treated with methanol to decompose excess of chromium trioxide, neutralized with concentrated hydrochloric acid, extracted with chloroform, washed with water and dried. Removal of the solvent and subsequent purification on alumina gave 70 mg. of an oil. Treatment of this oil (70 mg.) with hydrazine hydrate by usual way afforded 20 mg. of crystals, m. p. 198～202°C. Recrystallization from benzene gave yellow prisms, m. p. 206～207°C, identical with 2-amino-7-phenyltropone[13].

**Diels-Alder Reaction of II.**—A mixture of 200 mg. of II and 130 mg. (1.2 mol. equiv.) of maleic anhydride in 2 ml. of dry benzene was heated under reflux for 11 hr. On removal of the solvent 200 mg. of an oil was obtained which on standing for 10 days, gave 70 mg. of crystals, m. p. 145～170°C. Recrystallization from benzene gave white needles, m. p. 186～187°C.

Found: C, 71.88; H, 4.53. Calcd. for $C_{17}H_{14}O_4$: C, 70.33; H, 4.86%. $\lambda_{max}^{MeOH}$ 295 mμ (log ε: 2.43).

12) All the melting points are not crroected.

* On exposure in the air it decomposed to an oil.

**2-Isopropylcycloheptadienone (IX).**—A solution of 5 g. of tropone in 50 ml. of absolute ether was added at 0°C to a 2.2 mol. equiv. of Grignard reagent prepared from 13.36 g. of isopropyl bromide and 2.50 g. of magnesium in 40 ml. of absolute ether. The reaction mixture was treated as in the case of II. The resultant residue was distilled in vacuo to give three fractions: i) b. p. below 70°C (4 mmHg) $n_D^{15}$ 1.4870, 0.5 g.; ii) b. p. 70~75°C (4 mmHg), $n_D^{15}$ 1.4850, 4.4 g. (62%); iii) b. p. above 75°C (4 mmHg), small amount.

Found [for fraction (ii)]: C, 79.51; H, 9.05. Calcd. for $C_{10}H_{14}O$: C, 79.95; H, 9.39%.

**Hydrogenation of IX.**—2-Isopropylcycloheptadienone (IX) (300 mg.) was hydrogenated in 5 ml. of acetic acid at 1 atm. and 18°C with 10 mg. of prereduced platinum oxide catalyst. Ninty-five milliliters of hydrogen (2.0 mol. equv.) was taken up within 80 min. After removal of the catalyst, the mother liquor was diluted with water, extracted with petroleum ether, washed and dried. On evaporation of the solvent, 250 mg. of an oil was remained, which afforded semicarbazone, m. p. 170.5~171.5°C, undepressed on admixture with that of 2-isopropylcycloheptanone[13].

**Formation of 2-Isopropyltropone (X) by Bromination of IX.**—Bromine in carbon tetrachloride was added to a solution of 650 mg. of IX in 6.5 ml. of carbon tetrachloride by which 1.0 mol. equiv. bromine was absorbed. The reaction mixture was treated as in the case of II. Residual oil thus obtained was purified through its hydrochloride and then chromatographed on alumina, by which 160 mg. of brown oil was obtained. An ethanolic solution of this oil (160 mg.) was heated under reflux with 0.23 ml. of 80% hydrazine hydrate for 1 hr. Removal of the solvent followed by chromatography on alumina gave 100 mg. of crystals m. p. 40~50°C, $\lambda_{max}^{MeOH}$ 242, 336, 399 mμ, identical with that of 2-amino-7-isopropyltropone[9]. Hydrolysis of this crystals (100 mg.) with potassium hydroxide in aqueous ethanol afforded 60 mg. of an oil, having identical $R_f$ value with that of α-thujaplicin.

**Formation of 2-Isopropyltropone (X) by Dehydrogenation of IX with Selenium Dioxide.**—A solution of 1 g. of IX in 10 ml. of dioxane was heated under reflux with 440 mg. (1.2 mol. equiv.) of selenium dioxide for 1 hr. The reaction mixture was filtered to remove deposited selenium (150 mg.) which contains tarry matter and the mother liquor was concentrated. The resultant residue was dissolved in ether, washed with dilute silver nitrate solution and water, and dried. Removal of the solvent and subsequent distillation gave 550 mg. of an oil, b. p. ca. 80°C (2 mmHg), $\lambda_{max}^{MeOH}$ 233 mμ (log ε: 4.37), 312 mμ (log ε: 3.90). Heating of this oil (100 mg.) with 80% hydrazine hydrate (0.25 ml.) for 2 hr. under reflux afforded 90 mg. of yellow crystals, m. p. 40~60°C. Recrystallization from a mixture of benzene and petroleum ether gave yellow prisms, m. p. 88°C, undepressed on admixture with 2-amino-7-isopropyltropone[9].

13) S. Seto, *Sci. Repts. Tohoku Univ.*, I, 37, 292 (1953).

**2-Methylcycloheptadienone (XI).**—A solution of 2.4 g. of tropone in 30 ml. of absolute ether was added to 2.2 mol. equiv. of Grignard reagent prepared from 7.5 g. of methyl iodide and 1.2 g. of magnesium, at 0°C and the reaction mixture was treated as in the case of II. On evaporation of the solvent, 1.7 g. of pale yellow oil was obtained. Distillation in vacuo gave three fractions: i) b. p. below 60°C (2 mmHg), trace; ii) b. p. 60~65°C (2 mmHg), 1.0 g. (38%), $n_D^{14}$ 1.480; iii) b. p. above 65°C (2 mmHg), trace.

Found [for fraction (ii)]: C, 77.42; H, 8.04. Calcd. for $C_8H_{10}O$: C, 78.65; H, 8.25%.

**Hydrogenation of XI.**—XI (500 mg.) in 10 ml. of acetic acid was hydrogenated at 1 atm. and 18°C with prereduced platinum oxide. After 100 min., 122 ml. (2.2 mol. equiv.) of hydrogen was absorbed. The catalyst was removed by filtration and the filtrate was diluted with water, extracted with petroleum ether, washed and dried. Removal of the solvent gave a volatile oil, which gave semicarbazone, m. p. 118°C on allowing to stand with semicarbazide for 20 days at room temperature, undepressed 2-methylcycloheptanone[14].

**2-Methyltropone by Bromination of XI.**—To a solution of 500 mg. of XI in 10 ml. of carbon tetrachloride was added with stirring a solution of bromine into carbon tetrachloride, by which 1.4 mol. equiv. of bromine was easily absorbed. Treatment of the reaction mixture as in the case of IX afforded 500 mg. (60%) of crystals, decomp. 135°C, $\lambda_{max}^{MeOH}$ 232, 315 mμ, similar with that of 2-methyltropone hydrochloride. Neutralization of these crystals (100 mg.) with saturated sodium bicarbonate solution gave an oil, which afforded picrate, m. p. 126~127°C (60 mg.). Recrystallization from ethanol gave yellow crystals, m. p. 127~128°C, undepressed on admixture with those of 2-methyltropone[10].

**Formation of 2-Methyltropone by Dehydrogenation of XI with Selenium Dioxide.**—A solution of 300 mg. of XI in 3 ml. of dioxane was refluxed with 163 mg. (1.2 mol. equiv.) of selenium dioxide for half an hour. Deposited selenium contaminated with tar (80 mg.) was filtered off and similar treatment of the mother liquor as in the case of X afforded 180 mg. of an oil (60%) which gave picrate m. p. 127~128°C, identical with that of 2-methyltropone[10].

The authors thank to Professor T. Isobe for NMR spectra measurement and his kind discussions thereof. Expenses for the present series of experiments were defrayed by a Grant in Aid for Scientific Research from the Ministry of Education.

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14) D. N. Adamson and J. Kenner, *J. Chem. Soc.*, **1939**, 181.

# *Diels-Alder Reaction of Troponoids. II*[1]. *Adducts of Halotropones and Maleic Anhydride*

By Tetsuo Nozoe and Yasuo Toyooka

(Received on October 17, 1960)

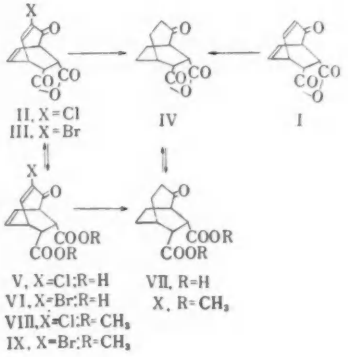
The Diels-Alder reaction of tropone and maleic anhydride has been reported from our laboratory[1]. Tropone gives a normal endo-cis adduct I more readily than tropolone, presumably owing to the property of enhanced unsaturation.

In the present paper the authors wish to report the Diels-Alder reactions of halotropones. It was found that 2-chloro- and 2-bromotropone give normal adducts in good yield, whilst 2, 7-dibromo- and 2, 4, 7-tribromotropone fail to give the adducts resulting in the complete recovery of the materials started with.

## Results

The heating of 2-chlorotropone or 2-bromotropone with two molar equivalents of maleic anhydride in dry xylene effected reaction, affording the adduct II or III in a yield of around 65~85%. The ultraviolet absorption spectra of II and III are shown in Fig. 1.

Catalytic hydrogenation of the adduct, II or III, in ethyl acetate with palladium charcoal as a catalyst, results in the absorption of three molar equivalents of hydrogen respectively both forming the same halogen-free tetrahydro compound IV, which showed no depression of the melting point on admixture with each other and with tetrahydro compound obtained from I. These facts not only offer an important clue to the structure of II and III but also prove the configurations of II and III being the same as I. Actually the infrared spectrum of IV obtained from II or III coincides perfectly with the one of tetrahydro compound obtained from I.




Treatment of the adduct II or III with hot water results in facile hydrolysis and dibasic acid V or VI is formed. The acids V and VI are known to be dibasic from their analytical value and titration. The decomposition points of V and VI are the same as the melting points of II and III respectively. These are considered to be due to the facial dehydrations of V and VI. Actually the heating of V and VI at 200~220°C under a reduced pressure result in the formations of II and III and such facts naturally indicate that the two carboxyls are in cis configuration.

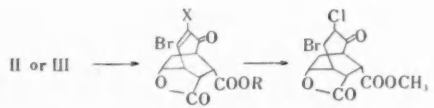
The halogen-free tetrahydro compound IV is also easily hydrolyzed and forms a dibasic acid VII which undergoes facile dehydration as in the case of V and VI. Catalytic hydrogenation of unsaturated dibasic acids V or VI in water, with palladium charcoal as a catalyst, results in absorption of three molar equivalents of hydrogen to form VII. Methylation of these three dibasic acids, V, VI and VII, with diazomethane affords dimethyl esters, VIII, IX and X. It has been found, however, that the reactions of V and VI with excess diazomethane also afford compounds VIII of $C_{11}H_{15}O_5N_2Cl$ and IX of $C_{14}H_{15}O_5N_2Br$. These compounds seem to be the same ones obtained in the case of dibasic acid of I and to have a pyrazol ring at the double bond of $\alpha\beta$-unsaturated ketone system[1]. All of the dimethyl esters, VIII, IX and X, easily form crystalline 2, 4-dinitrophenylhydrazones.

Bromination of the adduct II or III in aqueous solution by the method of Alder-Stein results in addition to the double bond and bromolactone XI or XII is obtained in a good yield. Titration of XI and XII shows them to be a monobasic acid, and the presence of a carboxyl and a $\gamma$-lactone is also indicated from the infrared spectral values listed in Table I.

1) Part I of this series: T. Nozoe, T. Mukai, T. Nagase and Y. Toyooka, This Bulletin, 33, 1247 (1960).

Table I. Infrared spectral values of several adducts and their derivatives ($cm^{-1}$)

| | I | II | III | Bromo-$\gamma$-lactone of I | XI | XII |
|---|---|---|---|---|---|---|
| 5-Membered acid anhydride ($\nu_{C=O}$) | 1840<br>1780 | 1875<br>1850<br>1785 | 1875<br>1840<br>1785 | | | |
| $\alpha\beta$-Unsaturated ketone ($\nu_{C=O}$) | 1665 | 1690 | 1680 | 1675 | 1685 | 1685 |
| C=C of $\alpha\beta$-unsaturated ketone ($\nu_{C=C}$) | 1625 | 1630<br>1605 | 1630<br>1595 | | 1655<br>1615 | 1610 |
| $\gamma$-Lactone ($\nu_{C=O}$) | | | | 1770 | 1780 | 1780 |
| Carboxylic acid ($\nu_{C=O}$) | | | | 1745 | 1710 | 1735 |
| Carboxylic acid ($\nu_{OH}$) | | | | 3320 | 3300 | 3350 |




XI, X=Cl;R=H
XII, X=Br;R=H
XIII, X=Cl;R=$CH_3$

XIV

Methylation of XI with diazomethane afforded monomethyl ester XIII. Catalytic hydrogenation of XIII on palladium charcoal in ethyl acetate results in absorption one molar equivalent of hydrogen and crystalline saturated bromolactone XIV is formed.

## Discussion

Bathochromic shifts in the ultraviolet maxima of II and III, 12~19 m$\mu$, respectively, from that of I, are best explained by the $\alpha$-substitution of halogen on the $\alpha\beta$-unsaturated carbonyl system, in accordance with Woodwards' rule (calcd. values: 242 m$\mu$ for II, 250 m$\mu$. for III).

Similar kinds of shifts are observed in the infrared spectra (cf. Table I). It is safely assumed, therefore, that the addition of maleic anhydride has taken place at C-4 and C-7 of 2-halotropone.

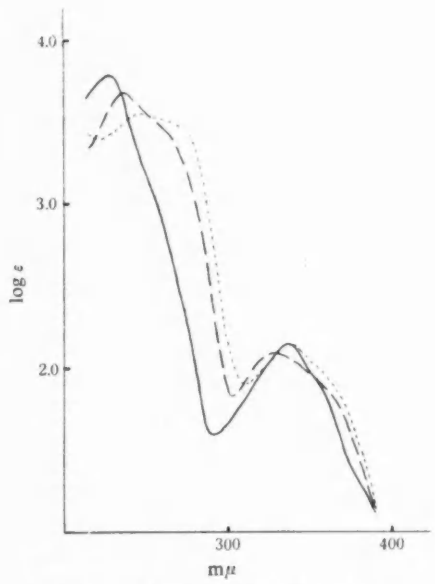



Fig. 1. —— (I) —— (II) ---- (III).

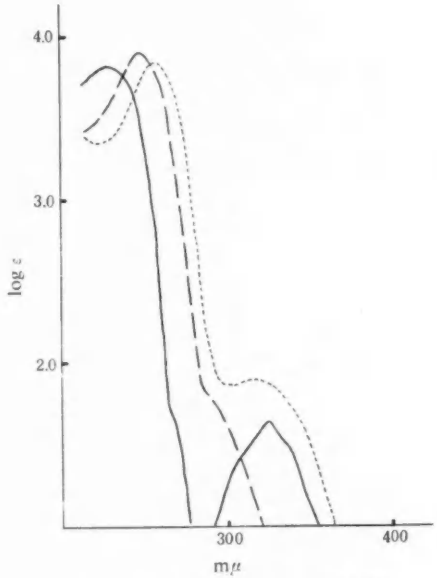



Fig. 2. —— Bromo-$\gamma$-lactone of (I)
—— (XI) ---- (XII).

It is clear from the foregoing experiments, that both II and III have the endo-cis configuration. Thus tetrahydro compound IV obtained by catalytic hydrogenation II and III is identical with the tetrahydro compound from I.

Products, XI and XII, formed by Alder-Steins' bromination of II and III still have $\alpha\beta$-unsaturated carbonyl system (cf. Fig. 2) indicating that the addition of BrOH occurred on the isolated double bond. This is also supported by the strong band at 1780 $cm^{-1}$ ($\gamma$-lactone) in both XI and XIII in their infrared spectra (cf. Table I).

Thus, the structure of bromolactones must be like the ones indicated in the figures.

## Experimental

**Preparation of Adduct II.**—The solution which contained 2.80 g. of 2-chlorotropone and 3.90 g. of maleic anhydride dissolved in 40 cc. of dry xylene was refluxed on an oil bath (175~180°C) for 24 hr. Standing overnight at room temperature, 3.18 g. of pale yellow seeds were separated. Several recrystallizations afforded colorless needles, m. p. 208~209°C.

Found: C, 55.58; H, 2.90. Calcd. for $C_{11}H_7O_4Cl$: C, 55.35; H, 2.09%.

**Preparation of IV.**—To the solution of 720 mg. of II dissolved in 80 cc. of ethyl acetate, 500 mg. of 5% palladium charcoal was added and was hydrogenated at ordinary temperature and pressure. The absorption of hydrogen was quite slow and 203 cc. of hydrogen (3 mol. equiv.) was absorbed for 2 days. After filtration of the catalyst the solvent was distilled off completely, the residue afforded colorless small needles, m. p. 191~192°C, 320 mg. by several recrystallizations from acetone-ethyl acetate mixture.

Found: C, 63.48; H, 5.63. Calcd. for $C_{11}H_{12}O_4$: C, 63.45; H, 5.81%. $\lambda_{max}^{MeOH}$ m$\mu$ (log $\varepsilon$): 291 (1.80).

Mixed melting point test with the tetrahydro adduct of I showed no depression.

**Preparation of V.**—Warming the suspension of 640 mg. of II in 50 cc. water on a boiling water bath, II was gradually dissolved. After evaporation to half volume and cooling in an ice bath, 620 mg. of V, as colorless leaflets separated. Although V has the same melting point to II, it melted in saturated sodium bicarbonate solution with effervescence, and neutralization titration value coincided to the dibasic one.

Found: C, 48.19; H, 3.97. Calcd. for $C_{11}H_{11}O_6Cl$: 48.09; H, 4.03%. $\lambda_{max}^{MeOH}$ m$\mu$ (log $\varepsilon$): 248 (3.60), 337 (2.19).

Heating of V in phosphorus pentoxide vacuum desiccator for two days, V changed to II.

**Preparation of VIII.**—To the solution of 550 mg. of V dissolved in 30 cc. of ethyl acetate, two molar equivalents of diazomethane ethereal solution was added dropwise. After several hours the solvent was distilled off completely, the residue afforded colorless fine powders, m. p. 165~169°C, 550 mg. Several recrystallizations gave colorless fine crystals, m. p. 172~173°C, 410 mg.

Found: C, 54.87; H, 4.87. Calcd. for $C_{13}H_{13}O_6Cl$: C, 58.87; H, 4.60%. $\lambda_{max}^{MeOH}$ m$\mu$ (log $\varepsilon$): 240 (3.74), 330 (1.01).

*2,4-Dinitrophenylhydrazone of VIII.*—To the solution of 80 mg. of VIII dissolved in 10 cc. of methanol, the mixture of 60 mg. of 2,4-dinitrophenylhydrazine, 0.1 cc. of concentrated sulfuric acid, 0.4 cc. of water and 1.3 cc. of methanol was added, then was refluxed on a water bath for 1.5 hr. Cooling in an ice bath 80 mg. of deep red fine crystals were separated. Several recrystallizations from a small amount of methanol afforded deep red fine crystals, m. p. 154°C, 50 mg.

Found: C, 50.86; H, 3.79; N, 12.38. Calcd. for $C_{19}H_{17}O_9N_4$: C, 49.09; H, 3.69; N, 12.05%. $\lambda_{max}^{MeOH}$ m$\mu$ (log $\varepsilon$): 261 (4.05), 370 (4.42).

**Preparation of VII.**—(A) *By Catalytic Hydrogenation of V.*—To the solution of 550 mg. of V dissolved in 70 cc. of water, 50 mg. of 5% palladium charcoal was added and the mixture was hydrogenated at ordinary temperature and pressure. The absorption of hydrogen was slow and 139 cc. (3.1 mol. equiv.) of hydrogen was absorbed. After the catalyst was filtered, off the solvent was removed completely, the residue afforded colorless powders (VII), d. p. 172.5°C, 350 mg. by several recrystallizations from small amount of water.

Found: C, 58.39; H, 5.94. Calcd. for $C_{11}H_{14}O_5$: C, 58.40; H, 6.24%. $\lambda_{max}^{MeOH}$ m$\mu$ (log $\varepsilon$): 292 (1.81).

(B) *By Hydrolysis of IV.*—Two hundred milligrams of IV was dissolved in 10 cc. of water, and then the solution was condensed to 1/3 volume on a boiling water bath. Colorless powders (VII), d. p. 173°C, 150 mg. were separated out on cooling.

Either VII obtained by (A) or (B) changed to IV on heating at 150°C in vacuum phosphorus pentoxide desiccator.

**Preparation of X.**—To the solution of 270 mg. of VII dissolved in 4 cc. of methanol, two molar equivalents of diazomethane ethereal solution was added dropwise. After several hours the solvent was removed completely, the residue afforded pale yellow oil, which failed to crystallize.

*2,4-Dinitrophenylhydrazone of X.*—The solution which contained 250 mg. of X and 200 mg. of 2,4-dinitrophenyl hydrazine dissolved in 5 cc. of methanol, 0.5 cc. of concentrated sulfuric acid, and 0.5 cc. of water was refluxed on a water bath for 1 hr. Orange crystals were separated. Several washings with hot methanol raised the melting point to 89°.

Found: C, 52.23; H, 4.90; N, 12.94. Calcd. for $C_{19}H_{22}O_9N_4$: C, 52.53; H, 5.10; N, 12.90%. $\lambda_{max}^{MeOH}$ m$\mu$ (log $\varepsilon$): 229 (4.19), 361 (4.33).

**Bromination of V: Preparation of XI.**—To the solution of 550 mg. of V dissolved in 40 cc. of water, 320 mg. of bromine was added dropwise under stirring. The color of the solution changed slowly to pale yellow and then colorless crystals were separated. After standing overnight 160 mg. of XI, d. p. 243°C, in colorless granules were obtained.

Found: C, 39.37; H, 2.27. Calcd. for $C_{11}H_8O_5BrCl$: C, 39.37; H, 2.41%.

**Preparation of XIII.**—To the solution of 440 mg. of XI dissolved in 20 cc. of ethyl acetate the calculated amount of diazomethane ethereal solution was added dropwise. After several hours the solvent

was removed and residue gave colorless crystals, m. p. 195~198°C, 450 mg. Several recrystallizations from methanol raised the melting point to 201~202°C.

Found: C, 41.40; H, 2.88. Calcd. for $C_{12}H_{10}O_5 \cdot BrCl$: C, 41.23; H, 2.88%.

**Preparation of XIV.**—To the solution of 250 mg. of XIII dissolved in 60 cc. of ethyl acetate, 100 mg. of 5% palladium charcoal was added and the mixture was hydrogenated at ordinary temperature and pressure. Eighteen cc. of hydrogen was absorbed (1.15 mol. equiv.). After filtration of the catalyst the solvent was distilled off, the residue afforded colorless powders, m. p. 219~222°C, 240 mg. Several recrystallizations from methanol raised the melting point to 230~232°C.

Found: C, 41.25, H, 3.17. Calcd. for $C_{12}H_{12}O_5 \cdot BrCl$: C, 40.99; H, 3.44%.

**Preparation of III.**—The solution which contained 370 mg. of 2-bromotropone and 400 mg. of maleic anhydride dissolved in 4 cc. of dry xylene was refluxed on an oil bath for 13 hr. Standing overnight in a cool place yellow crystals, m. p. 223~228°C, 410 mg. were separated. Recrystallization from acetone-ethyl acetate mixture raised the melting point to 232~233°C (350 mg.).

Found: C, 46.78; H, 2.40. Calcd. for $C_{11}H_7 \cdot O_4Br$: C, 46.67; H, 2.49%.

**Hydrolysis of III.**—After dissolving 200 mg. of III in 10 cc. of water, the solution was evaporated to 1/2 volume on a boiling water bath. Colorless scales, d. p. 233°C, 180 mg. were separated on cooling.

Found: C, 44.00; H, 2.86. Calcd. for $C_{11}H_9 \cdot O_5Br$: C, 43.88; H, 3.10%. $\lambda_{max}^{MeOH}$ mμ (log ε): 248 (3.60), 337 (2.16).

**Bromination of VI.**—To the solution of 570 mg. of VI dissolved in 100 cc. of water, 320 mg. of bromine was added dropwise at room temperature under stirring. After standing overnight colorless granules, d. p. 246°C, 500 mg. were separated. Several recrystallizations from methanol-ethyl acetate mixture afforded colorless crystals, d. p. 257°C, 320 mg.

Found: C, 34.85; H, 2.04. Calcd. for $C_{11}H_5 \cdot O_2Br_2$: C, 34.77; H, 2.12%.

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# *Reaction of Hydrogen Peroxide on Fatty Acid Esters under Pressure. III. Oxidation of Methyl 9, 10-Dihydroxystearate*

By Hiromu KAMEOKA

(Received June 4, 1960)

The reaction of hydrogen peroxide on methyl oleate[1] and on saturated fatty acid methyl esters[2] under pressure has already been reported in detail. The present research was carried out with the intention of finding the kinds of compounds formed by the action of hydrogen peroxide on methyl 9, 10-dihydroxystearate produced by the oxidation of methyl oleate with potassium permanganate and of following up the course of the reaction in the oxidation with hydrogen peroxide as mentioned above.

When methyl oleate is oxidized under pressure by the use of hydrogen peroxide, the position between 9 and 10 having a double bond is oxidized. In this case, however, the formation of 9, 10-dihydroxystearic acid is not observed, but substances coming from cutting off the carbon chain of methyl oleate at the position between 9 and 10 are formed. Moreover, various lower homologues of monobasic and dibasic fatty acid are formed. These are presumably produced by the oxidation at the other position of the carbon chain.

Expecting that the position between 9 and 10 where a double bond exists initially in methyl oleate is most liable to be oxidized in the oxidation of methyl 9, 10-dihydroxystearate and consequently $C_9$-aldehyde and $C_9$-fatty acid may be formed with relatively good yields. Methyl 9, 10-dihydroxystearate was subjected to the action of a 30% hydrogen peroxide solution under pressure.

The results obtained in this reaction were like those in the oxidation of saturated fatty acid methyl esters under a similar condition, excepting that the position between 9 and 10 was oxidized.

## Experimental

**Methyl 9, 10-Dihydroxystearate.**—Commercial oleic acid was separated into solid acid and liquid acid through the lead-salt-ethanol process. The liquid acid was converted into lithium salt. This

1) H. Kameoka, *J. Chem. Soc. Japan, Ind. Chem. Sec.* (*Kogyo Kagaku Zasshi*), **63**, 741 (1960).
2) H. Kameoka, ibid., **63**, 744 (1960).

lithium salt, insoluble in a 50% ethanol solution, was filtered out and then changed to free fatty acid. The free fatty acid was subjected to the fractional distillation in a current of carbon dioxide gas three times. The distillate at the distillation temperature of 163~165°C/1 mmHg was oxidized in an aqueous alkaline solution of potassium permanganate, and sulfur dioxide gas was passed into the solution. After filtrating the aqueous solution, the remaining white substance was thoroughly washed with petroleum ether. This substance was recrystallized from a solution of 80% ethanol several times. The resulting crystalline substance having its melting point at 131~132°C and its neutralization value at 177.0 was esterified with methanol and sulfuric acid. The ester was recrystallized from an 80% ethanol solution once more. The ester thus prepared had an acid value 0.0, a saponification value 167.2, a hydroxyl value 334.5 and a melting point 104~105°C, and it was used as the sample of this research.

**Hydrogen Peroxide.**—A 30% solution was used.

**Reaction under Pressure.**—The sample (methyl 9, 10-dihydroxystearate) and a 30% hydrogen peroxide solution were enclosed in an autoclave (a capacity of 100 cc.) made of stainless steel, having an electromagnetic stirrer. The initial pressure in each test was maintained at 0 kg./cm². By heating the autoclave, the inside temperature and pressure of it were raised. In this case, heating was controlled in such a way that it may take about 1.5 hr. to reach the temperature shown in Table I, and the pressure was also raised up to the values given in Table I. The reaction time indicates the length of time held within the range of these temperatures and pressures. The conditions of reaction are shown in Table I.

**Treatment of the Reaction Products.**—Having been allowed to stand overnight after the completion of the reaction, the autoclave was opened. The reaction mixture was taken into a separating funnel. The interior of the autoclave was then thoroughly washed with distilled water and petroleum ether. The washing solutions used were also taken into the separating funnel. The content in the separating funnel was extracted with petroleum ether. In this way the content was separated into the soluble portion [A] and the insoluble portion [B].

As the petroleum ether soluble portion [A], a rather viscous oily substance was obtained after entirely removing the petroleum ether by distillation. This substance, after its constants were measured,

Table I. Conditions of reaction

| Reaction No. | Sample wt., g. | 30% $H_2O_2$ g. | Initial press. kg./cm² | Press. kg./cm² | Temp. °C | Final press. kg./cm² | Reaction time min. | Stir. r. p. m. |
|---|---|---|---|---|---|---|---|---|
| 1 | 5.0 | 50 | 0 | 65~ 80 | 100~110 | 40 | 90 | 60 |
| 2 | 5.0 | 50 | 0 | 110~120 | 130~140 | 75 | 120 | 60 |
| 3 | 5.0 | 60 | 0 | 130~145 | 138~146 | 65 | 120 | 60 |
| 4 | 5.0 | 50 | 0 | 115~120 | 145~155 | 70 | 180 | 60 |
| 5 | 6.8 | 50 | 0 | 110~125 | 145~155 | 65 | 180 | 60 |
| 6 | 10.2 | 50 | 0 | 100~110 | 125~140 | 60 | 120 | 60 |
| 7 | 10.2 | 50 | 0 | 120~135 | 140~150 | 60 | 180 | 60 |

Table II. Table of the systematic separation of the reaction products

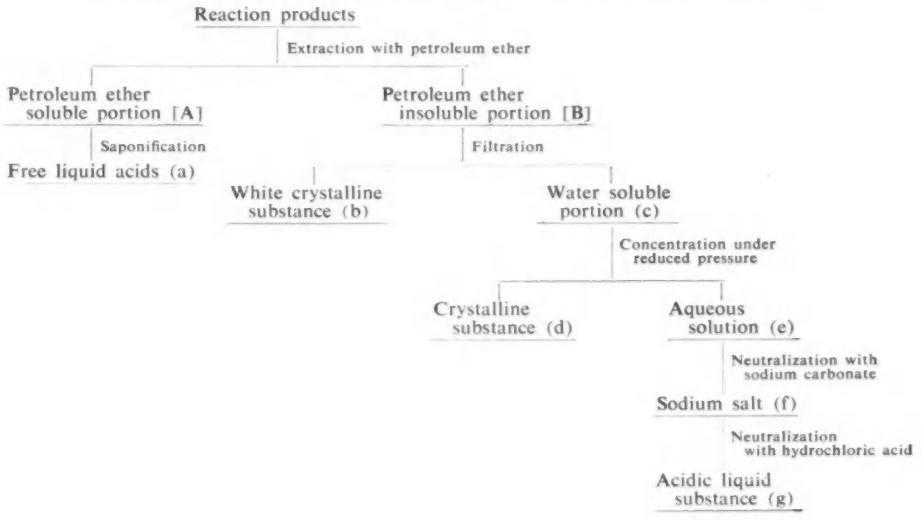

TABLE III. FRACTION (a). FREE ACID (Reaction No. 7, sample of fractional dist. 1.8 g.)

| Fraction No. | Temp. of dist., °C/mmHg | Yield g. | N. v. | $R_f$ value | Fatty acids detected |
|---|---|---|---|---|---|
| 1 | ~170 | 0.2 | 605.3 | * 0.69, 0.82 | $C_3$, $C_4$-monobasic |
| 2 | 170~210 | 0.3 | 461.9 | * 0.82, 0.90, 0.96 | $C_4$, $C_6$, $C_8$-monobasic |
| 3 | 120~140/15 | 0.6 | 365.6 | * 0.90, 0.95<br>△ 0.59 | $C_6$, $C_8$-monobasic<br>$C_9$-monobasic |
| 4 | 140~160/15 | 0.4 | 305.3 | △ 0.66, 0.59, 0.54 | $C_8$, $C_9$, $C_{10}$-monobasic |
| 5 | 160~170/15 | 0.2 | 279.6 | △ 0.54, 0.44 | $C_{10}$, $C_{12}$-monobasic |
| 6 | Residue | 0.1 | — | △ 0.44 | $C_{12}$-monobasic |

Paper chromatography: * Monobasic $C_2$~$C_8$-fatty acid, through the hydroxamic acid process[3]. —One-dimensional ascending method; development solvent, butanol saturated with water; filter paper, Toyo. No. 2; development temperature, 30°C; coloring matter, 10% ferric chloride-ethanol solution. △ Members above monobasic $C_8$-fatty acid, through the 2,4-dinitrophenylhydrazide process[4]. —One-dimensional ascending method; development solvent, methanol-acetic acid-tetraline; stationary phase, tetraline; filter paper, Toyo. No. 2; development temperature, 30°C; coloring matter, 0.5 N potassium hydroxide ethanol solution.

TABLE IV. FRACTION (d). CRYSTALLINE SUBSTANCE
(through fractional crystallization, sample 2.5 g.)

| Cryst., No. | Yield, g. | N. v. | M. p., °C | $R_f$ value | Fatty acids detected |
|---|---|---|---|---|---|
| 1 | 0.8 | 943.9 | 180~183 | □ 0.67 | $C_4$-dibasic |
| 2 | 1.2 | 763.5 | 150~153 | □ 0.88 | $C_6$-dibasic |
| 3 | 0.4 | 651.0 | 110~131 | □ 0.88<br>○ 0.48 | $C_6$-dibasic<br>$C_9$-dibasic |
| 4 | 0.1 | — | — | □ 0.89<br>○ 0.48 | $C_6$-dibasic<br>$C_9$-dibasic |

Paper chromatography: □ Dibasic $C_2$~$C_6$-fatty acid, through the chloroform-acetic acid-water process[5]. —One-dimensional ascending method; development solvent, chloroform-acetic acid-water; filter paper, Toyo. No. 2; development temperature, 20°C; coloring matter, 0.1% bromocresol-green-ethanol solution. ○ Members above dibasic $C_6$-fatty acid, through the petroleum ether-chloroform-acetic acid process[6]. —One-dimensional ascending method; development solvent, petroleum ether-chloroform-acetic acid; filter paper, Toyo. No. 2; development temperature, 20°C; coloring matter, 0.1% bromocresolgreen-ethanol solution.

was saponified to convert it into free fatty acids (a).

The petroleum ether insoluble portion [B] was spontaneously separated to a white crystalline substance (b) and a water-soluble portion (c). The crystalline substance b, which was filtered out from c, was washed with distilled water several times and the washing water used was added to c. The whole of c was concentrated under 20 mmHg pressure. In this case c was separated into an aqueous solution (e) and the crystalline substance (d). The aqueous solution (e) showing itself to be acidic was neutralized by the use of a 1% aqueous solution of sodium carbonate. By concentrating this solution, a solid sodium salt (f) was obtained. The salt f was acidified with hydrochloric acid, and then extracted with a large amount of ether. After removing the ether by distillation, an acidic liquid substance (g) was obtained. Examination was made about the substances separated through the process mentioned above respectively. In Table II, the treating procedure of the reaction products are represented.

**Petroleum Ether Soluble Portion [A].** — This portion is a rather viscous oily substance and is fragrant. It being presumable that pelargonic aldehyde produced by the breakage between the positions of 9 and 10 may exist in the portion A, this portion was tested to see whether it may form an adduct of sodium bisulfite by the ordinary process or not. However, this test did not give any positive result. Then, a 2 N hydrochloric acid solution of 2,4-dinitrophenylhydrazine was added to the portion A. In this case, a very small amount of yellowish orange precipitates was obtained, the amount of which was not sufficient for identification.

This portion A was next converted to the free acid by saponification with a 5% alcoholic potassium hydroxide solution. The free acid thus obtained was subjected to fractional distillation and the constants of the distillates were measured. The result of Reaction No. 7 is given in Table III.

Each of the portion A obtained in Reactions No. 1—No. 6 was similarly subjected to fractional distillation. Almost the same result as that of Reaction No. 7 was obtained. Moreover, as the hydroxyl value of the portion A was all zero, this portion has no hydroxy compound.

3) Y. Inoue and M. Noda, *J. Japan Oil Chemist's Soc. (Yukagaku)*, **1**, 136 (1952).
4) Y. Inoue and M. Noda, *Bull. Agr. Chem. Soc. Japan*, **19**, 214 (1955).
5) M. Kobayashi, *J. Japan Oil Chemist's Soc. (Yukagaku)*, **4**, 53 (1955).
6) M. Kobayashi, ibid., **5**, 85 (1956).

Table V. Fraction (g). Acidic liquid substance
(sample of the fractional distillation, 1.5 g.)

| Fraction No. | Temp. of dist., °C | Yield g. | N. v. | $R_f$ value | Fatty acids detected |
|---|---|---|---|---|---|
| 1 | ~120 | 0.5 | 930.6 | * 0.50 | $C_2$-monobasic |
| 2 | 120~145 | 0.4 | 759.6 | * 0.50, 0.68 | $C_2$, $C_3$-monobasic |
| 3 | 145~165 | 0.4 | 633.0 | * 0.68, 0.82 | $C_3$, $C_4$-monobasic |
| 4 | Residue | 0.2 | 595.1 | * 0.82 | $C_4$-monobasic |

Paper chromatography: * Hydroxamic acid process[3].

**Petroleum Ether Insoluble Portion [B].**—*Crystalline Substance (d) Contained in the Water Soluble Portion (c).*—The substance is assumed to be dibasic acid from its good solubility in water, and good crystallizable property. This crystalline substance was fractionally crystallized from a 10% ethanol solution, and the crystals shown in Table IV were obtained in the case of Reaction No. 7.

The fraction d obtained in Reactions No. 1—No. 6 was similarly subjected to the fractional crystallization with almost the same result as that mentioned above. In cases of the oxidizing conditions as in Reactions No. 1, No. 3 and No. 6, the formation of low members of dibasic acid such as $C_2$ and $C_3$ was observed.

Each acid thus separated has nearly an equal neutralization value to the corresponding pure acid. Furthermore, no depression of the melting point was observed when each acid was subjected to the mixed melting point determination.

*The Sodium Salt (f) and the Acidic Liquid Substance (g).*—The substance g obtained from the salt f was fractionally distilled, and inquiries were made about the respective fractions. The result of Reaction No. 7 is shown in Table V.

In the result shown above, the neutralization values of fractions No. 1, No. 2 and No. 3 were nearly equal to those of acetic, propionic and butyric acids, 934.5, 757.4 and 637.1, respectively. Accordingly it may be confirmed that the main components of these fractions are acetic, propionic and butyric acids. The results of the fractional distillation of g obtained in Reactions No. 1—No. 6 were almost the same as the above. Furthermore, from the result of paper chromatography[4] (hydroxamic acid process: $R_f$ value 0.90) it was observed that small quantities of monobasic $C_5$ fatty acid were contained in g obtained in Reactions No. 1—No. 3.

*White Crystalline Substance (b).*—This substance is insoluble in water and petroleum ether. From its saponification value, hydroxyl value and melting point in addition to the insolubility nature mentioned above, this substance seemed to be non-oxidized methyl 9,10-dihydroxy stearate (Table VI). Furthermore, because of its slightly higher acid value and the considerably wide range of its melting point, the formation of free 9,10-dihydroxystearic acid due to the partial hydrolysis of the ester is presumable. Accordingly, this was saponified, and the melting point of 130~132°C and the neutralization value of 175~176 were obtained for the resulting acid. No depression of the melting point was observed when mixed with 9,10-dihydroxystearic acid. Moreover, the substance b was subjected to paper chromatography[5,6]. No existence of dibasic acid in it, however, was observed.

## Results

The yields and constants of the separated substances, and the results concerning them in paper chromatography are summarized in Table VI.

As shown in Table VI, lower members of monobasic acid were mainly detected in the portion A. Water soluble lower members of monobasic and dibasic acid and unchanged methyl 9, 10-dihydroxystearate were detected in the portion B. Further, it was found that under the reaction conditions as in Reactions No. 3, No. 4 and No. 5, more than 80% of the methyl 9, 10-dihydroxystearate used was oxidized.

## Discussion

In the present experiments, the reaction products, except the nonoxidized substance, had no hydroxyl value. This fact indicates that the hydroxyl group of the initial sample was removed during the oxidation with hydrogen peroxide.

Furthermore, from the fact that monobasic $C_9$-acid and dibasic $C_9$-acid were present in the portion A and also in the fraction d, it is clear that the positions of 9 and 10 where the hydroxyl group was initially located are oxidized. The production of the only small quantity of $C_9$-compounds by breakage at this position is probably explained by the consideration that this position is first attacked by oxygen and $C_9$-compounds are produced, but the resulting substances are immediately oxidized, and the compounds of smaller carbon numbers are formed. It is evident that lower monobasic acids than $C_{10}$ are liable to be oxidized with hydrogen peroxide[7]. Alternatively, it is considered that other positions of the carbon chain are simultaneously split by the oxidation. This fact is clearly found from the formation of $C_{12}$, $C_{10}$-acids and/or lower acids. In case

7) H. Kameoka, ibid., 9, 351 (1960).

TABLE VI. REACTION PRODUCTS

| Reaction No. | Petroleum ether soluble portion [A] | | | Petroleum ether insoluble portion [B] | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Water soluble portion (c) | | | | | | | White crystalline substance (b) | | | | |
| | | | | Crystalline substance (d) | | | Aqueous solution (e) | | | | | | | | |
| | | | | | | | | Acidic liquid substance, g. | | | | | | | |
| | Yield g. | N. v. | Fatty acids detected *, △ | Yield g. | N. v. | Acids detected □, ○ | Na-salt (f) g. | Yield g. | N. v. | Acids detected, * | Weight g. | A. v. | S. v. | M. p., °C | Acids detected |
| 1 | 1.5 | 235.7 | $C_{18}$, $C_{12}$, $C_{10}$, $C_9$, $C_8$, $C_6$, $C_4$-monobasic | 0.6 | 589.3 | $C_2$, $C_3$, $C_4$, $C_6$, $C_9$-dibasic | 1.3 | 0.3 | 320.9 | $C_2$, $C_3$, $C_4$, $C_6$-monobasic | 2.5 | 72.1 | 177.6 | 110～119 | Methyl 9,10-dihydroxy-stearate |
| 2 | 1.0 | 307.1 | $C_{18}$, $C_{12}$, $C_{10}$, $C_9$, $C_8$, $C_6$, $C_4$-monobasic | 1.1 | 659.9 | $C_4$, $C_6$, $C_9$-dibasic | 1.9 | 1.0 | 559.7 | $C_2$, $C_3$, $C_4$, $C_6$-monobasic | 1.7 | 55.8 | 188.4 | 89～96 | 〃 |
| 3 | 1.2 | 346.1 | $C_{12}$, $C_{10}$, $C_9$, $C_8$, $C_4$, $C_3$, $C_2$-monobasic | 1.8 | 603.2 | $C_2$, $C_3$, $C_4$, $C_6$, $C_9$-dibasic | 2.8 | 1.4 | 735.2 | $C_2$, $C_3$, $C_4$, $C_6$-monobasic | 0.5 | 43.0 | 186.8 | 94～104 | 〃 |
| 4 | 1.2 | 306.6 | $C_{12}$, $C_{10}$, $C_9$, $C_8$, $C_4$, $C_3$, $C_2$-monobasic | 1.7 | 594.8 | $C_4$, $C_6$, $C_9$-dibasic | 1.9 | 0.9 | 783.6 | $C_2$, $C_3$, $C_4$-monobasic | 1.0 | 47.1 | 180.6 | 88～104 | 〃 |
| 5 | 1.7 | 321.5 | $C_{12}$, $C_{10}$, $C_9$, $C_8$, $C_6$, $C_4$, $C_3$-monobasic | 2.1 | 615.0 | $C_4$, $C_6$, $C_9$-dibasic | 2.8 | 1.4 | 755.0 | $C_2$, $C_3$, $C_4$-monobasic | 1.4 | 39.8 | 176.5 | 92～104 | 〃 |
| 6 | 1.9 | 331.2 | $C_{12}$, $C_{10}$, $C_9$, $C_8$, $C_6$, $C_4$-monobasic | 2.0 | 605.1 | $C_3$, $C_4$, $C_6$, $C_9$-dibasic | 3.4 | 1.7 | 743.0 | $C_2$, $C_3$, $C_4$-monobasic | 4.3 | 40.5 | 179.8 | 93～104 | 〃 |
| 7 | 2.3 | 332.4 | $C_{12}$, $C_{10}$, $C_9$, $C_8$, $C_6$, $C_4$, $C_3$-monobasic | 3.2 | 590.6 | $C_4$, $C_6$, $C_9$-dibasic | 3.8 | 1.8 | 780.6 | $C_2$, $C_3$, $C_4$-monobasic | 2.5 | 43.6 | 181.5 | 89～104 | 〃 |

Paper chromatography: * hydroxamic acid process[3]; △ 2,4-dinitrophenylhydrazide process[4]; □ chloroform-acetic acid-water process[5]; ○ petroleum ether-chloroform-acetic acid process[6].

of the formation of $C_{12}$, $C_{10}$-acids, hydroxy acids were not obtained. The mechanism concerning no formation of hydroxy acid has not yet been available.

The formation of considerably large amount of $C_4$- and $C_6$-dibasic acids was observed. These products should result from (i) the further oxidation of the substances produced by the breakage of the bond between 9 and 10, and (ii) the secondary oxidation of monobasic $C_{12}$- and $C_{10}$-acids which are produced by the direct oxidation of methyl 9, 10-dihydroxystearate. The formation of considerably quantities of dibasic acids will be ascribed to the oxidation of the methyl group of the lower monobasic acids produced by the direct oxidation mentioned above. Moreover, in case of the oxidizing conditions as in Reactions No. 1, No. 3 and No. 6, the formation of lower members of dibasic acid such as $C_2$ and $C_3$ was recognized. These $C_2$- and $C_3$-dibasic acids may probably be formed under other conditions of reaction. Because of the easy decomposition of these dibasic acids, however, they will be decomposed when the reaction conditions are intense. Furthermore, it is considered that the formation of various lower homologues of fatty acid is due to the same oxidation course as that of the saturated fatty acid methyl ester[2] irrespective of the hydroxyl groups present in the sample molecule.

In short, in the oxidation of methyl 9, 10-dihydroxystearate with hydrogen peroxide, the following reactions will be presumed. That is, the positions 9, 10 containing hydroxyl groups are first oxidized, and the products of such oxidation are subjected to the secondary oxidation, and also there occurs the other reaction following the course of the oxidation similar to that of the saturated acid.

**Summary**

Methyl 9, 10-dihydroxystearate is oxidized with a 30% hydrogen peroxide solution, under such conditions as the mole ratio of methyl 9, 10-dihydroxystearate to hydrogen peroxide is one to fifteen or more, the reaction time 2 hr., the temperature 138～155°C, and the pressure 110～145 kg./cm$^2$. Also, it was recognized that 80% or more of methyl 9, 10-dihydroxystearate was oxidized.

As the oxidation products, acetic, propionic, butyric, caproic, caprilic, pelargonic, caprinic and lauric acids were obtained as monobasic acids, and oxalic, malonic, succinic, adipic and azelaic acids were also produced as dibasic acids. Especially, succinic and adipic acids were obtained with good yield.

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# *Polymerization of Allyl Chloride by Ziegler's Catalyst**

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In recent years many papers have been published on the stereospecific polymerization of $\alpha$-olefins by Ziegler's catalyst. However it is well known that the catalyst, by itself, has little effect on the stereospecific polymerization of monomers containing any heteroatom, such as oxygen, nitrogen, sulfur or halogen, except only vinyl butyl ether, a stereospecific polymerization of which was found by Natta[1].

An attempt was made on the polymerization by Ziegler's type catalysts with allyl chloride as a monomer containing heteroatom. Since allyl chloride was first polymerized by Staudinger[2] to a syrupy low polymer, many investigations were done on the polymerization of this monomer, but no solid polymer has been obtained due to the "degradative chain transfer"[3] in its radical polymerization.

By Ziegler's type catalysts allyl chloride

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1) G. Natta et al., *Angew. Chem.*, **71**, 205 (1959).

2) H. Staudinger and Th. Tleitmann, *Ann.*, **480**, 92 (1930).

3) P. D. Bartlett and R. Alschul, *J. Am. Chem. Soc.*, **67**, 812, 816 (1945). F. M. Lewis and F. R. Mayo, *J. Am. Chem. Soc.*, **76**, 457 (1954).

reacted rather rapidly at low temperatures with evolution of hydrogen chloride and gave a solid polymeric material. In the polymer produced the chlorine content was very much reduced for polyallyl chloride $[C_3H_5Cl]_n$ and indications of some unsaturation were observed. It was found that the polymerization took place only with catalysts having Al-Cl bond. Furthermore, the polymerization was accelerated by the presence of a small amount of benzene, which incorporated in the polymer.

On the basis of these results it was concluded that the polymerization of allyl chloride with Ziegler's type catalysts does not proceed by an anionic mechanism which is characteristic of these catalysts, but occurs with a some Friedel-Crafts type reaction caused by compounds such as $Et_2AlCl$, $EtAlCl_2$ or $AlCl_3$ formed in the reaction mixture. Also a cationic mechanism is likely to contribute simultaneously to the polymerization.

Similar results were obtained with the polymerization using allyl fluoride, allyl bromide, and 3, 3, 3-trichloropropene-1 as the monomer, respectivey.

## Experimental

**Materials.** — *Allyl Chloride.* — Commercial allyl chloride was purified by distillation and a fraction of b. p. 44.0~45.0 C was used.

*Allyl Bromide.* — Synthesized according to Kamm and Marvel[4]. B. p. 70°C.

*Allyl Iodide.* — Prepared from allyl chloride and sodium iodide as described by Letsinger and Traynham[5]. B. p. 48°C/108 mmHg.

*Allyl Fluoride.*—Prepared from silver fluoride and allyl iodide[6], and collected in a trap cooled in a dry ice-acetone bath. An infrared absorption spectrum of the gaseous sample was shown in Fig. 2.

*3,3,3-Trichloro-1-propene.* (*Nippon Soda Co.*). — Distilled and a fraction of b. p. 50~53°C/80 mmHg was used.

*n-Hexane.* — Purified in the usual manner and stored over metallic sodium.

*Triethylaluminum.* — Supplied by Mitsui Chem. Ind. Co. and was used as a solution in *n*-heptane.

*Titanium Tetrachloride.*—Supplied by Osaka Titanium Co. and was used as a solution in *n*-heptane.

**Apparatus.** — A 50 ml. five-necked flask[7] fitted with a thermometer, a stirrer, a nitrogen gas inlet tube and two silicone rubber caps was used as the polymerization vessel. Catalyst components, monomer, and solvent were introduced into the vessel through rubber caps with a hypodermic syringe.

**Preparation of Catalysts.**—After the vessel was flushed by dry nitrogen, 20 ml. of *n*-hexane and 0.25 g. of titanium tetrachloride were introduced. With boiling the mixture gently, 0.15 g. of $AlEt_3$ was slowly added dropwise, and heating was continued for further 5 min. and cooled. After precipitating the solid catalyst complex the supernatant liquid was removed by a syringe under dry nitrogen. The catalyst was washed three times with 20 ml. of *n*-hexane, and then 20 ml. of *n*-hexane and 0.15 g. of $AlEt_3$ was added.

Other catalysts of Ziegler's type were prepared in the same manner but the wash procedure was omitted.

**Polymerization.** — The catalyst was cooled to the polymerization temperature in a dry ice-acetone bath and with stirring the monomer was slowly added dropwise. The reaction was exothermic and the heat evolved spontaneously at or after the addition of the monomer, when deep cooling was required to keep the temperature constant. After three to five hours the reaction was stopped by adding 10 ml. of methanol containing a small amount of hydrochloric acid and the polymer was precipitated by pouring the mixture into about 300 ml. of methanol. After standing overnight the polymer was collected and washed with methanol, and dried in vacuo. The polymer was reprecipitated from its benzene solution by methanol.

Allyl fluoride was polymerized as follows. The monomer gas was introduced by a gas inlet tube bubbling through the catalyst suspension and the unreacted monomer was recycled through a trap cooled in dry ice-acetone bath.

**Double Bond Titration of Polymer.** — A known amount of polymer (about 0.05 g.) was dissolved in 8 ml. of carbon tetrachloride in a 100 ml. glass stoppered flask and 2 ml. of 0.5 N bromate-bromide solution and 1.3 ml. of 10% sulfuric acid were added. After shaking the mixture vigorously for three minutes 2 ml. of 20% aqueous potassium iodide solution were added and again the mixture was shaken vigorously for a minute. The liberated iodine was titrated by 0.1 N sodium thiosulfate solution with starch as an indicator.

**Reduction of Polymer with $LiAlH_4$.**—A polymer of allyl chloride (0.25 g.) polymerized by $AlEt_3$-$TiCl_4$ catalyst and containing 20.81% by weight of chlorine was reacted with 0.4 g. of $LiAlH_4$ in 30 ml. tetrahydrofuran. The reaction was carried out under dry nitrogen in a sealed tube with shaking for 150 hr. at 60°C. After cooling, the reaction mixture was poured into methanol containing nitric acid to decompose excess $LiAlH_4$. The precipitated polymer was collected, washed with methanol and dried in vacuo. The chlorine content of the product was 7.50% (by wt.).

## Results

The results were summarized in Tables I, II and III.

During the polymerization, especially in its initial stage, usually a sudden increase in temperature of the reaction mixture and a evolution of hydrogen chloride were observed, while the color of the catalyst turned to reddish brown gradually.

4) O. Kamm and C. S. Marvel, "Organic Syntheses", Coll. Vol. 1, (1956), p. 27.
5) R. L. Letsinger and J. G. Traynham, *J. Am. Chem. Soc.*, **70**, 2818 (1948).
6) M. H. Meslans, *Compt. rend.*, **111**, 882 (1890).
7) S. Murahashi, S. Nozakura, M. Sumi and K. Hatada, This Bulletin, **32**, 1094 (1959).

TABLE I. POLYMERIZATION OF ALLYL CHLORIDE WITH ZIEGLER'S CATALYST

Monomer: 5 ml. (4.70 g.), Catalyst: $AlEt_3$ 0.30 g. + $TiCl_4$ 0.25 g. ($AlEt_3/TiCl_4$=2 mol./mol.), Solvent: *n*-Hexane.

| Polymerization | | | Polymer | | | | |
|---|---|---|---|---|---|---|---|
| Temp. °C | Time hr. | Solvent ml. | Yield % | Cl-content*1 % | M. p. °C | $\eta_{sp}/C$*5 dl./g. | Double bond mol./$C_3$-unit |
| 20 | 3 | 15 | 29.3 | 12.53*2 | 73~ 75 | 0.043 | 0.16 |
| 0 | 5 | 20 | 9.9 | 20.61 | 80~ 81 | 0.035 | — |
| −10 | 5 | 20 | 9.1 | 19.55 | 85~ 86 | 0.040 | — |
| −20 | 5 | 20 | 9.6 | 21.40*3 | 89~ 91 | — | 0.17 |
| −30 | 5 | 45 | 7.1 | 18.26*4 | 105~108 | 0.081 | 0.13 |
| −70 | 170 | 20 | 1.5 | 22.25 | 73~ 75 | — | — |

*1 Theoretical value for poly(allyl chloride) $[-CH_2-CH(CH_2Cl)-]_n$: 46.33%.
*2 C, 74.64%; H, 9.20%; corresponding to $C_3H_{4.4}Cl_{0.17}$.
*3 C, 69.30%; H, 8.71%; corresponding to $C_3H_{4.3}Cl_{0.32}$.
*4 C, 73.21%; H, 8.66%; corresponding to $C_3H_{4.3}Cl_{0.25}$.
*5 Benzene solution (C=0.5 g./dl.) at 30°C.

TABLE II. POLYMERIZATION OF ALLYLHALIDES WITH ZIEGLER'S CATALYST

Catalyst: $AlEt_3$ 0.30 g. + $TiCl_4$ 0.25 g. ($AlEt_3/TiCl_4$=2 mol./mol.)
Solvent: *n*-Hexane.

| Monomer ml. | Polymerization | | Solvent ml. | Polymer | | | | |
|---|---|---|---|---|---|---|---|---|
| | Temp. °C | Time hr. | | Yield g. | Halogen content, % Found | Halogen content, % Theoretical | M. p. °C | $\eta_{sp}/C$(30°C) dl./g. |
| $CH_2$=CH-$CH_2$F 1.0*1 | 50 | 45 | 20 | 0.030 | — | 31.63 | — | — |
| 3.2*1 | 25 | 7 | 25 | 0.050 | 3.2 | | 97~ 98 | — |
| 1.2*1 | −20 | 2.5 | 25 | 0.030 | 1.5 | | 75~ 77 | — |
| $CH_2$=CH-$CH_2$Br 3.5 | −20 | 5 | 20 | 0.255 | 30.00*2 | 66.05 | 85~ 87 | 0.025 |
| $CH_2$=CH-$CH_2$I 3.0 | −20 | 5 | 20 | trace | — | 75.55 | — | — |
| $CH_2$=CH-$CCl_3$ 2.0 | 20 | 5 | 20 | 0.180 | 35.28 | 73.14 | 135~140 | — |

*1 The quantities were shown as volumes at −80°C.
*2 C, 61.14%; H, 7.49%; corresponding to $C_3H_{4.4}Br_{0.22}$. Double bond 0.12 mol./$C_3$-unit.

The polymer obtained was a powder colored in faint yellow, having a melting point between 70~110°C and soluble in benzene, toluene, and tetrahydrofuran. Generally the chlorine content of the polymer was less than a half of the theoretical value (46.33%) for polyallyl chloride $[-CH_2-CH(CH_2Cl)-]_n$. The low viscosity of the polymer solution is indicative of the fairly low molecular weight of the polymer.

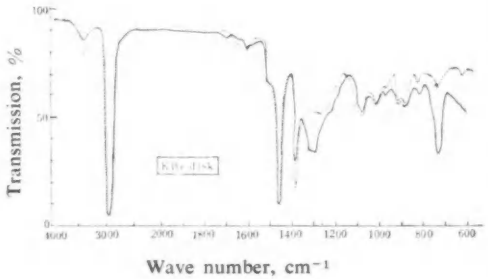


Fig. 1. Infrared absorption spectra of the polymer of allyl chloride (——) and its reduction product with $LiAlH_4$ (·····).

Infrared spectra of a typical sample of the polymer and of its reduction product by lithium aluminum hydride were shown in Fig. 1. The absorption bands arising from C-Cl linkage appeared at 730 $cm^{-1}$ and about 1300 $cm^{-1}$, and the intensities were decreased with the reduced polymer. At 1378 $cm^{-1}$ and 1460 $cm^{-1}$ are located the absorption bands due to the presence of methyl and methylene groups, respectively. The former increased its intensity relatively to the latter by the reduction of the polymer, indicating the presence of $-CH_2Cl$ groups in the polymer. The bands in a region between 800 $cm^{-1}$ and 1000 $cm^{-1}$ seems to be characteristic of various types of double bonds. In addition to this spectral data the double bond titration of the polymer showed about 0.15 mol. unsaturations per monomer unit in general (Tabel I).

These polymers were shown to be amorphous by their X-ray diffractions.

The chlorine content of the polymer was independent of the polymerization temperature in the range between 0°C and −70°C, while the conversion was strongly depressed at −70°C. The melting point of the polymer and its solution viscosity in benzene decreased slightly with raising the polymerization temperature (Table I).

The polymerizations of allyl fluoride, allyl bromide and 3, 3, 3-trichloro-1-propene by $AlEt_3$-$TiCl_4$ catalyst gave similar solid polymers as obtained from allyl chloride and their halogen contents were also much less than the theoretical values calculated for the monomeric units (Table II). The polymers of allyl fluoride and allyl bromide gave the similar infrared absorption spectra as that given by the polymer of allyl chloride, but the very weak band at 1070 $cm^{-1}$ was considered to be of the C–F linkage in the former polymer (Fig 2). The band appeared to arise from the C–Br linkage was located at 569 $cm^{-1}$ in the polymer of allyl bromide.

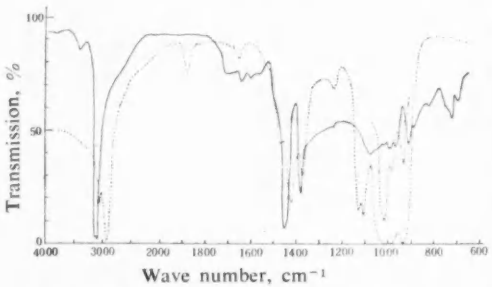


Fig. 2. Infrared absorption spectra of gaseous allyl fluoride (·····) and its polymer (—— KBr disk).

Allyl iodide gave no polymer by $AlEt_3$-$TiCl_4$ catalyst under the same condition as in the polymerization of allyl chloride.

Various types of catalysts were examined for the polymerization of allyl chloride (Table III). Among the Ziegler's type catalysts used, all the compounds having Al–Cl linkage, either the linkage was original or formed from the catalyst components, were capable of polymerizing allyl chloride. However, the catalysts such as $AlEt_3$-$Ti(OBu)_4$, LiBu-$TiCl_4$ and $ZnEt_2$ (ether solution)-$TiCl_4$ gave no polymer under similar or even more drastic conditions. It should be noted, however, that the catalyst prepared from $AlEt_3 \cdot Et_2O$ and $TiCl_4$ hardly polymerized allyl chloride, although the catalyst might have possibly Al–Cl linkage in it.

Of the catalyst for cationic polymerization, what possessed Al–Cl linkage also functioned as catalyst for the polymerization of allyl chloride, while no polymer was obtained with $TiCl_4$ and $BF_3 \cdot Et_2O$. On the other hand, all the basic catalysts examined, such as LiBu, $ZnEt_2$(ether solution) and $AlEt_3$, had no catalytic activity for the polymerization.

It was found that an addition of benzene to the reaction mixture caused remarkable increase in the polymer yield (Table III) and also in the evolution of hydrogen chloride during the polymerization. An infrared absorption spectrum of the yielded polymer (Fig. 3) showed absorption bands due to skeletal vibrations of a benzene ring at 1605

TABLE III. POLYMERIZATION OF ALLYL CHLORIDE WITH VARIOUS CATALYSTS

Monomer: 3.5 ml., Solvent: *n*-Hexane 25 ml., Polymerization temperature: −20°C, Polymerization time: 5 hr.

| Catalyst*6 | Benzene g. | Polymer: Yield % | Cl-content % | M. p. °C | $\eta_{sp}/C$*5 dl./g. | Double bond (mol./$C_3$-unit) |
|---|---|---|---|---|---|---|
| $AlEt_3$-$TiCl_3$ | 0 | 5.0*1 | 14.79 | 94～ 95 | 0.050 | — |
| $AlEt_3$-$VOCl_3$ | 0 | 6.4 | 18.71 | 86～ 89 | 0.043 | — |
| $AlEt_3 \cdot Et_2O$-$TiCl_4$ | 0 | 0.8 | — | — | — | — |
| $Et_2AlCl$-$TiCl_4$ | 0 | 10.8 | 19.20 | 83～ 85 | 0.050 | — |
| $Et_2AlCl$-$TiCl_4$ | 1.0 | 31.6*2 | 16.77 | 116～118 | 0.093 | 0.08 |
| $Et_2AlCl$ | 0 | 4.4 | 23.87 | 84～ 85 | 0.036 | — |
| $Et_2AlCl$ | 1.3 | 29.6*3 | 15.05 | 99～102 | 0.072 | 0.06 |
| $AlCl_3$ | 0 | 9.9 | 23.60 | 79～ 80 | 0.033 | — |
| $AlCl_3$ | 1.0 | 44.7*4 | 17.66 | — | — | — |

*1 Reaction time: 4 hr.

*2, *3, *4 Benzene-insoluble fractions were 31.7, 11.5, and 16.8%, based on the total amounts of polymers, respectively. The following data described above were obtained on the soluble fractions.

*5 Benzene solution (C = 0.5 g./dl.) at 30°C.

*6 The ratios of the two components were unity, except 0.2 of $AlEt_3/TiCl_3$.

$cm^{-1}$ and 1498 $cm^{-1}$, indicating an existence of a benzene ring in the polymer chain. Furthermore, a part of this polymer was not soluble in any usual organic solvents and had no melting point even above 300°C, and was assumed to be a cross-linked polymer through benzene nuclei. The soluble fraction of this polymer had a higher melting point, a higher solution viscosity and a lower chlorine content, compared with the polymer formed under the same condition but without benzene.

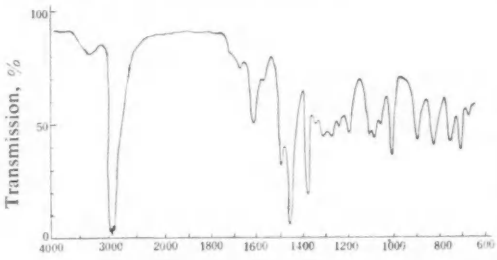


Fig. 3. Infrared absorption spectrum of the polymer of allyl chloride polymerized in the presence of benzene. KBr disk.

## Discussion

The results mentioned above reveals that the following features are involved in the polymerization of allyl chloride with Ziegler's type catalyst: a) An evolution of hydrogen chloride during the polymerization and a strongly reduced chlorine content of the resulting polymer. b) Only compounds containing Al–Cl bond such as $Et_2AlCl$, $EtAlCl_2$ and $AlCl_3$ function to polymerize allyl chloride. These compounds are powerful catalysts of Friedel-Crafts reaction. c) A marked increase in conversion with an addition of benzene to the system and an incorporation of benzene to the resulting polymer. d) An existence of double bonds in the polymer.

On the basis of these facts it is proposed that the Friedel-Crafts type reactions 1, 2 and 3 caused by a compound containing Al–Cl bond is essential in the polymerization of allyl chloride by Ziegler's type catalyst. It seems to be possible that a minor contribution of ordinary cationic processes 1 and 4 is involved and causes some complication in the reaction.

$$CH_2{=}CH{-}CH_2Cl + \overset{|}{Al}{-}Cl \longrightarrow CH_2{=}CH{-}\overset{+}{C}H_2\left[Cl{-}\overset{|}{Al}{-}Cl\right]^- \quad (1)$$

$$CH_2{=}CH{-}\overset{+}{C}H_2\left[Cl{-}\overset{|}{Al}{-}Cl\right]^- + CH_2{=}CH{-}CH_2Cl \longrightarrow CH_2{=}CH{-}CH_2{-}CH{=}CH{-}\overset{+}{C}H_2\left[Cl{-}\overset{|}{Al}{-}Cl\right]^- + HCl \quad (2)$$

or

$$CH_2{=}CH{-}CH_2{-}\underset{\underset{CH_2}{\|}}{C}{-}\overset{+}{C}H_2\left[Cl{-}\overset{|}{Al}{-}Cl\right]^- + HCl \quad (3)$$

$$CH_2{=}CH{-}\overset{+}{C}H_2\left[Cl{-}\overset{|}{Al}{-}Cl\right]^- + CH_2{=}CH{-}CH_2Cl \longrightarrow CH_2{=}CH{-}CH_2{-}CH_2{-}\overset{+}{C}H(CH_2Cl)\left[Cl{-}\overset{|}{Al}{-}Cl\right]^- \quad (4)$$

The reaction may proceed in such a manner as follows: a slow first stage of the reaction catalyzed by a small amount of original species having Al–Cl linkage, such as $Et_2AlCl$, $EtAlCl_2$ or $AlCl_3$, is followed by a faster reaction owing to a gradual accumulation of these catalyst compound generated by a reaction between $AlEt_3$ and hydrogen chloride liberated during the polymerization, and this finally leads to a violent rise of temperature of the reaction mixture.

The fact that the polymerization is strongly accelerated by adding a small amount of benzene to the system is a further evidence for the Friedel-Crafts type mechanism of the polymerization reaction. The benzene may undergo a variety of reaction, thus forming cross-linkages in some extent between polymer chains and giving a rather large amount of insoluble fraction of the polymer.

Methyl groups in the polymer may be produced by the reactions as following scheme.

$$\sim\!\!\sim\underset{\underset{CH_2}{\|}}{C}\!\!\sim\!\!\sim \xrightarrow{HCl} \sim\!\!\sim\underset{\underset{CH_3}{|}}{\overset{\overset{Cl}{|}}{C}}\!\!\sim\!\!\sim$$

$$\sim\!\!\sim\underset{\underset{CH_2Cl}{|}}{CH}\!\!\sim\!\!\sim \xrightarrow{Et_3Al\ etc.} \sim\!\!\sim\underset{\underset{CH_3}{|}}{CH}\!\!\sim\!\!\sim \quad \text{or} \quad \sim\!\!\sim\underset{\underset{C_3H_7}{|}}{CH}\!\!\sim\!\!\sim$$

In the case of $AlEt_3{\cdot}Et_2O{\cdot}TiCl_4$ catalyst, these components may also produce any compound such as $Et_2AlCl$, $EtAlCl_2$ or $AlCl_3$, but etherated. It is considered that the coordinated ether reduces the ionic character of the Al–Cl bond so strongly that the compound can not function as a catalyst for the Friedel-Crafts type reaction.

The authors wish to thank Mitsui Chem. Ind. Co. for the generous supply of triethylaluminum and Osaka Titanium Co. for titanium tetrachloride.

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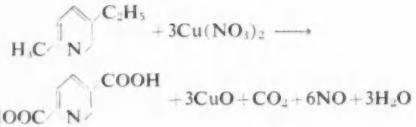
# *Oxidation of 2-Methyl 5-Ethyl Pyridine to Isocinchomeronic Acid*

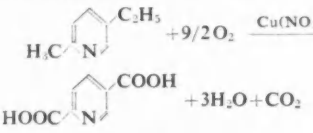
By Tokio KATO

(Received August 26, 1960)

In the preparation of isocinchomeronic acid (ICA) from 2-methyl 5-ethyl pyridine (MEP), several kinds of oxidizing reagents, such as sulfuric acid[1], selenium peroxide[2], nitric acid[3] and cupric nitrate[4] have been used. Cupric nitrate (with or without nitric acid) is said to give the highest yield of ICA among them, where this process consumes a large quantity of nitrate or nitric acid (more than 10 mol. as $NO_3$ to 1 mol. MEP oxidized).



MEP can not be oxidized with molecular oxygen as in the case of *p*-xylene with catalysts such as cobalt or manganese acetates. But the combined use of oxygen (a little more than theoretical moles for the oxidation of MEP) with cupric nitrate was found to be effective to obtain ICA (through its cupric salt) with a yield higher than 85 ml. % to MEP consumed, where the used cupric nitrate was easily recovered and reused.



## Experimental

**Materials.**—MEP of more than 98% purity was purchased from Carbide and Carbon Chem. Co. Ltd., and used without purification. Its specifications are as following; specific gravity ($20^\circ/20^\circ$), 0.918～0.922; b. p., 171～181°C (760 mmHg); water content, less than 0.2% by weight. Reaction vessel was 1 l. auto-clave (18:8 stainless steel) with magnetic stirrer.

**Oxidation.**—MEP, cupric nitrate (as 200 cc. aqueous solution) and oxygen were charged in the

TABLE I. REACTION VARIABLE IN THE OXIDATION OF MEP.

| Exp. No. | MEP mol. | $Cu(NO_3)_2$[a] mol. | Charged mol. ratio $Cu(NO_3)_2$/MEP | $N_2$[d]+$O_2$ atm. | $O_2$% by vol. | Duration min.[b] 180～200°C | 200～230°C |
|---|---|---|---|---|---|---|---|
| 1 | 0.149 | 0.79 | 5.30 | Not charged | | 10 | 200 |
| 2 | 〃 | 0.476 | 3.20 | 〃 | | 〃 | 〃 |
| 3 | 〃 | 0.155 | 1.04 | | | | |
| 4 | 0.197 | 0.203 | 〃 | 〃 | | 〃 | 〃 |
| 5 | 0.149 | 0.103 | 0.69 | 50 | 54 | 〃 | 130 |
| 6 | 〃 | 0.155 | 1.04 | 〃 | 55 | 3 | 100 |
| 7 | 〃 | 0.103[c5] | 0.69 | 〃 | 53 | 10 | 180 |
| 8 | 0.198 | 0.155 | 0.77 | 58 | 56 | 5 | 85 |
| 9 | 〃 | 〃 [c8] | 〃 | 〃 | 48 | 3 | 90 |
| 10 | 〃 | 〃 [c9] | 〃 | 〃 | 42 | 〃 | 120 |
| 11 | 0.197 | 0.203 | 1.04 | 〃 | 45 | 5 | 130 |
| 12 | 〃 | 〃 | 〃 | 〃 | 40 | 5 | 120 |
| 13 | 〃 | 〃 | 〃 | 50 | 44 | 〃 | 160 |
| 14 | 〃 | 〃 | 〃 | 53 | 50 | 30 | 95 |
| 15 | 〃 | 〃 | 〃 | 60 | 54 | 240 | 0 |
| 16 | 0.296 | 〃 | 0.69 | 90 | 48 | 30 | 180 |
| 17 | 〃 | 〃 [c16] | 〃 | 80 | 53 | 20 | 150 |

a) Used as 200 cc. aqueous solution in each experiments.
b) See Figs. 1, 2 and 3.
c) Recovered $Cu(NO_3)_2$ charged c5), c8), c9) and c16) mean recovered ones in Exps. No. 5, 8, 9 and 16 respectively.
d) Measured at 20°C before heating the vessel.

1) T. E. Jordan, *Ind. Eng. Chem.*, **44**, 332 (1952).
2) D. Jercher, *Chem. Ber.*, **88**, 156 (1955).
3) U. S. Pat. 2524957 (1950).
4) U. S. Pat. 2552268 (1951).

TABLE II. RESULTS OF EXPERIMENTS IN TABLE I

| Exp. No. | $O_2$ Consumed moles | mol. ratio $O_2$/MEP | $CO_2$ Produced moles | mol. ratio $CO_2$/MEP | Cupric Isocinchomronate moles×2[a], % | yield[b] | ICA Yield[b] % |
|---|---|---|---|---|---|---|---|
| 1 | Not charged | | 0.18 | 1.2 | Not charged | | 87 |
| 2 | 〃 | | 0.17 | 1.1 | 〃 | | 40 |
| 3 | 〃 | | 0.19 | 1.3 | 〃 | | 7 |
| 4 | 〃 | | 0.20 | 1.0 | 〃 | | 0 |
| 5 | 0.70 | 4.7 | 0.13 | 0.9 | 0.133 | 89 | 84 |
| 6 | 0.76 | 5.1 | 0.12 | 0.8 | 0.127 | 85 | 80 |
| 7 | 0·68 | 4.6 | 0.20 | 1.3 | 0.138 | 92 | 87 |
| 8 | 0.83 | 4.2 | 0.18 | 0·9 | 0.179 | 90 | 85 |
| 9 | 0.75 | 3.8 | 0.22 | 1.1 | 0.174 | 88 | 83 |
| 10 | 0.76 | 〃 | 0.24 | 1.2 | 0.179 | 90 | 85 |
| 11 | 0.87 | 4.4 | 0.20 | 1.0 | 0.180 | 91 | 86 |
| 12 | 0.80 | 3.9 | 0.16 | 0.8 | 〃 | 〃 | 〃 |
| 13 | 0.74 | 3.8 | 0.25 | 1.3 | 0.177 | 90 | 85 |
| 14 | 0.82 | 4.2 | 0.24 | 1.2 | 0.182 | 92 | 87 |
| 15 | 0.84 | 4.3 | 0.23 | 〃 | 0.181 | 〃 | 〃 |
| 16 | 1.27 | 〃 | 0.36 | 〃 | 0.278 | 94 | 88 |
| 17 | 1.25 | 4.2 | 0.33 | 1.1 | 0.279 | 〃 | 〃 |

a) 1 mol. of cupric salt is prepared from 2 mol. of MEP
b) Based upon consumed moles of MEP

TABLE III. FORMATION OF ICA FROM ITS CUPRIC SALT

| Exp. No. | Aqueous soln. of NaOH Concn. of NaOH % by wt. | gr. | Mol. ratio NaOH/ICA | Conditions Temp. °C | Duration hr. | Moles | ICA Yield[a] % by wt. |
|---|---|---|---|---|---|---|---|
| 1 | 10 | 300 | 4.9 | 95 | 1.0 | 0.141 | 93 |
| 2 | 〃 | 200 | 3.3 | 〃 | 〃 | 0.143 | 94 |
| 3 | 〃 | 100 | 1.6 | 〃 | 〃 | 0.064 | 42 |
| 4 | 〃 | 〃 | 〃 | 〃 | 3.0 | 0.053 | 35 |
| 5 | 5 | 400 | 3.3 | 〃 | 1.0 | 0.145 | 95 |
| 6 | 〃 | 300 | 2.5 | 〃 | 〃 | 0.143 | 94 |
| 7 | 〃 | 〃 | 〃 | 75 | 〃 | 0.144 | 95 |

a) Based upon the cupric salt consumed, and in each Exp. 0.076 mol. (30.0 g.) of the cupric salt was used.

autoclave, where oxygen was diluted to less than 60% by volume with nitrogen. In some experiment, oxygen was not charged, in order to compare their results with that of other experiments, in which oxygen was used. The vessel was heated and its temperature was kept at 180~230°C, until oxygen was sufficiently absorbed to the oxidate and its pressure stopped dropping.

After the vessel was cooled to room temperature, the content of oxygen and carbon dioxide in the blowing gas was measured. The reaction product was filtered, where the deposit obtained was submitted to elementary analysis after being washed with water and dried in an air oven.

A certain quantity of the deposit was mixed and stirred with hot alkali aqueous solution, and copper was filtered off as cupric oxide from the solution.

Sodium salt of ICA (very soluble in water) formed in the filtrate was neutralized with concentrated aqueous hydrochloric acid, and white deposit liberated at pH 1.8~2.0, was also submitted to elementary analysis after being washed with water and dried in the air oven.

## Results and Discussion

Reaction variables in the oxidation of MEP and their results were shown in Tables I and II respectively.

With no oxygen charged as in Exps. 1—4, the cupric salt of I.C.A. in the reaction product was not pure, being mixed with other cupric salts such cupric oxide, cupric hydroxide, and cupric nitrite.

Furthermore the yield of ICA fell markedly with decrease of cupric nitrate charged.

In Exps. 5—17 with oxygen used, the deposits obtained were uniformly found to be pure cupric isocinchomeronate (2 mol. of isocinchomeronate combined with 1 mol. of $Cu^{2+}$).

Found: C, 42.09; H, 2.22; N, 7.02; Cu, 16.25. Calcd. for $(C_7H_3O_4N)_2Cu$: C, 42.49; H, 2.04; N, 7.08; Cu 16.05%.

With decrease of cupric nitrate charged, the yield was not lowerd (always not less than

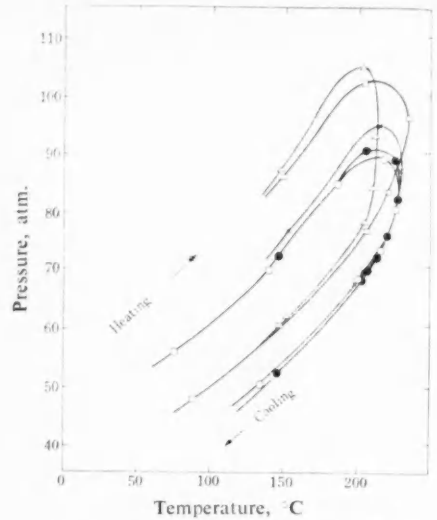



Fig. 1. Absorption of oxygen in the oxidation of MEP.
(Exp. Nos. 5—9) plotted per 30 min.
—○— No. 5 —△— No. 8
—×— 〃 6 —□— 〃 9
—●— 〃 7

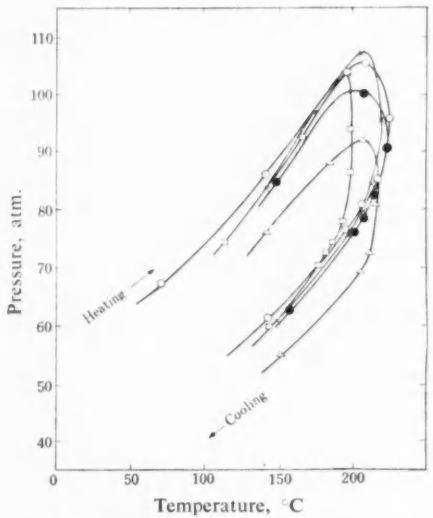



Fig. 2. Absorption of oxygen in the oxidation of MEP.
(Exp. Nos. 10—15) plotted per 30 min.
—○— No. 10 —△— No. 14
—×— 〃 11,12 —□— 〃 15
—●— 〃 13

85 mol.% to MEP consumed), and any trace of nitrogen oxide or nitrogen dioxide was not detected in the reaction product and blowing gas. Cupric nitrate used was easily

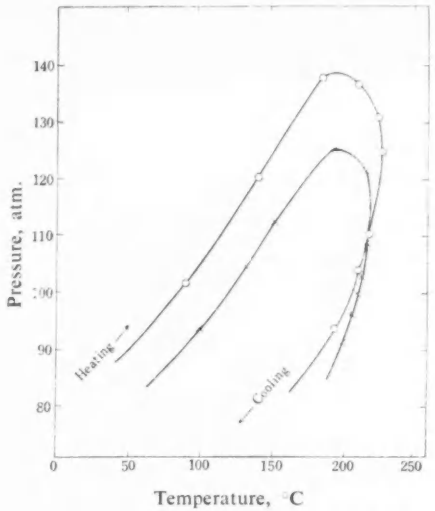



Fig. 3. Absorption of oxygen in the oxidation of MEP.
(Exp. 16 and 17) plotted per 30 min.
—○— No. 16 —×— No. 17

recovered by cupric oxide or cupric hydroxide being dissolved in the recovered filtrate and it was reused as in Exps. 7, 9, 10 and 17.

As shown in Figs. 1, 2 and 3, oxygen was absorbed at 180~230°C, where overheating was found to cause violent explosion. Molar ratio of oxygen consumed and carbon dioxide formed to that of MEP oxidized were approximately consistent to the theoretical values, 4.5 and 1.0 respectively. Based upon the results in Tables I, II and Figs. 1—3, the oxidation of MEP to cupric isocinchomeronate is considered to proceed as following;

$$C_2H_5(C_5NH_3)CH_3+9/2\,O_2+1/2\,Cu(NO_3)_2 \rightarrow$$
$$1/2(HOOC_5NH_3COO)_2Cu+3H_2O+CO_2+HNO_3$$

and oxygen only is consumed to oxidize MEP.

ICA prepared from its cupric salt, as shown in Table III, and its dimethyl ester melted at 237 and 164°C respectively, both of which agree with the values in the literature[5]. Isocinchomeronic acid in Table II.

Found: C, 49.98; H, 2.96; N, 8.34. Calcd. for $C_7H_5O_4N$: C, 50.34; H, 3.01; N, 8.38%.

The author is grateful to Dr. H. Sobue, Professor of Tokyo University, Dr. A. Tomita, Chief of the Laboratory Institute, and Dr. Y. Tsunoda for their valuable advice.

*Laboratory Institute*
*Tokai Electrode Mfg. Co.*
*Fujisawa, Kanagawa-ken*

5) Beilstein, Band 12, p. 154, 155.

# *The Crystal Structure of p-Aminobenzenearsonic Acid**

By Akira SHIMADA

(Received August 6, 1960)

The crystal structure of benzenearsonic acid has recently been reported by the present author[1] to reveal the molecular configuration of an organoarsenic compound and the hydrogen-bond formation in this crystal. In connection with the above work, the crystal structure of *p*-aminobenzenearsonic acid, $H_2N \cdot C_6H_4AsO(OH)_2$, was undertaken as a part of a program concerned with the crystal chemistry of organoarsenic compounds.

This study has another interest, since the sodium salt of this acid has always proved of great value in medicine under the name of "Atoxyl".

## Experimental

Suitable crystals for X-ray work were selected from the specimens kindly prepared and supplied by Professor H. Nakata of Konan University. They were colorless, transparent needles with a long dimension in the *b* direction. Oscillation and Weissenberg photographs were taken with Cu $K_\alpha$ radiation, and they showed that the unit cell is monoclinic with the following dimensions:

a=7.35 Å, b=6.35 Å, c=8.81 Å, and $\beta=101°$

It was already shown by Gilta[2] that this crystal belongs to the monoclinic system with the axial ratios, $a:b:c=1.162276:1:1.393499$, and the monoclinic angle, $\beta=101°20'$. The axial ratios given above by the morphological method can be compared with, 1.157 : 1 : 1.387, the values derived by the X-ray measurement. Two formula units per unit cell results in a calculated density 1.786 g. cm$^{-3}$**.

The only extinction rule was found for $(0k0)$ with $k$ odd, which indicates the probable space group $P2_1$ with the fact that a symmetry plane is not permissible, and this was confirmed in the course of the structure analysis. All the intensities were estimated visually with a calibrated scale, by making use of the mutiple-film technique. The data were recorded from small crystals [cross sections with rectangular dimensions; 0.18×0.11 mm. for $(h0l)$, and 0.09×0.21 mm. for $(0kl)$], and

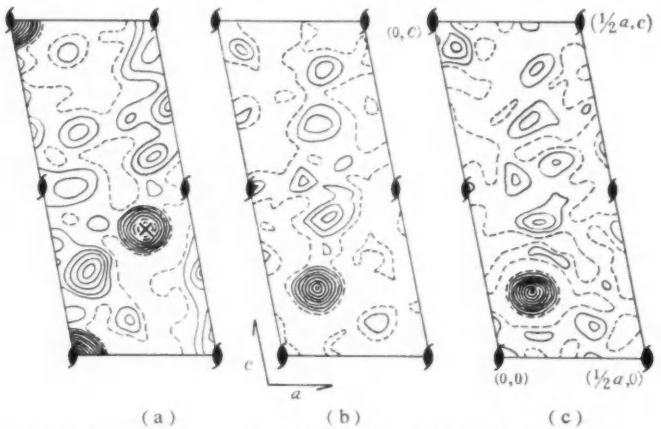



Fig. 1. (a) The Patterson projection, $P(UW)$, along the *b* axis, the rotation peak due to arsenic atoms being marked by a cross. Contours at arbitrary scale. (b) The minimum function, $M_2(XZ)$, derived from the rotation peak in Fig. 1a. (c) The electron-density projection, $\rho_1(XZ)$, for comparison with $M_2(XZ)$ in Fig. 1b. Contours at arbitrary scale.

* The major part of this paper was read at the 13th Annual Meeting of the Chemical Society of Japan, Tokyo, April, 1960.

1) A. Shimada, This Bulletin, **32**, 309 (1959); A. Shimada, ibid., **33**, 301 (1960).

2) G. Gilta, *Bull. soc. chim. Belges*, **32**, 19 (1923).

** The density was measured to be 1.9571 g. cm$^{-3}$ by Lorenz and Schmidt (*Z. anorg. u. allgem. Chem.* **112**, 269 (1920)), and the author obtained the value of 1.85 g. cm$^{-3}$ by floatation in bromoform and carbon tetrachloride mixture. These observed values are higher than the calculated value, but it seems certain that the unit cell contains two formula units.

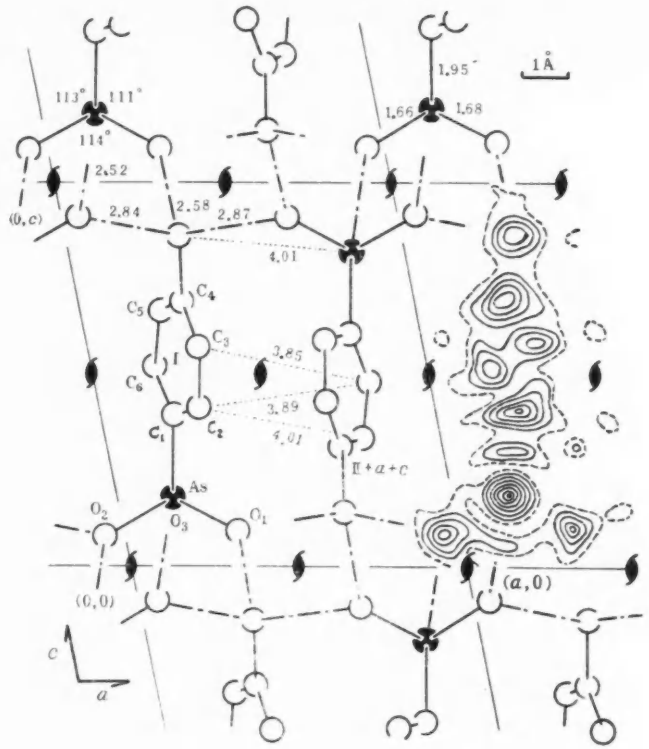



Fig. 2. The structure and the electron-density projection along the *b* axis, with bond angles, intra- and intermolecular distances (Å). Contours at intervals of $2\,e\,Å^{-2}$, starting at $2\,e\,Å^{-2}$ (broken lines), except the arsenic atom, where contours are at intervals of $10\,e\,Å^{-2}$. Dot-dash lines indicate hydrogen bonds.

no absorption corrections were applied. The corrections for polarization and Lorentz factors were made in the usual way.

### Structure Determination

The structure has been determined by making use of the heavy atome technique. The Patterson projection $P(UW)$ onto the (010) plane was first synthesized, because the b axis is the shortest and the projection of the structure has a center of symmetry. This Patterson projection $P(UW)$, as shown in Fig. 1a, seemed to give some clues to the outline of molecules due to vectors from the heavy arsenic atom to the lighter atoms in addition to the location of the arsenic atom due to the large rotation peak near the origin. Consequently, we set up the minimum function $M_2(XZ)$ based upon this rotation peak. At the same time, the electron-density projection $\rho_1(XZ)$ was synthesized, the Fourier terms being the observed structure amplitudes whose signs were determined only by the coordinates of an arsenic atom. It will be seen that there is a good correspondence between $M_2(XZ)$ and $\rho_1(XZ)$ as shown in Figs. 1b and 1c, and they are sufficient to give the approximate coordinates of lighter atoms. With these maps as a start, a sequence of electron-density projections were synthesized to make clear all of the atomic positions except hydrogen atoms.

Although the projection onto (100) plane has no center of symmetry, the electron-density projections were constructed by the successive refining, referring to the Patterson projection onto (100) plane and the refined electron-density projection onto (010) plane. The final electron-density projections are shown in Figs. 2 and 3, and the final coordinates are listed in Table I, being refined by the difference syntheses at later stages.

In the calculation of structure factors, McWeeny's scattering curves[3] for nitrogen

3) R. McWeeny, *Acta Cryst.*, **4**, 513 (1951).

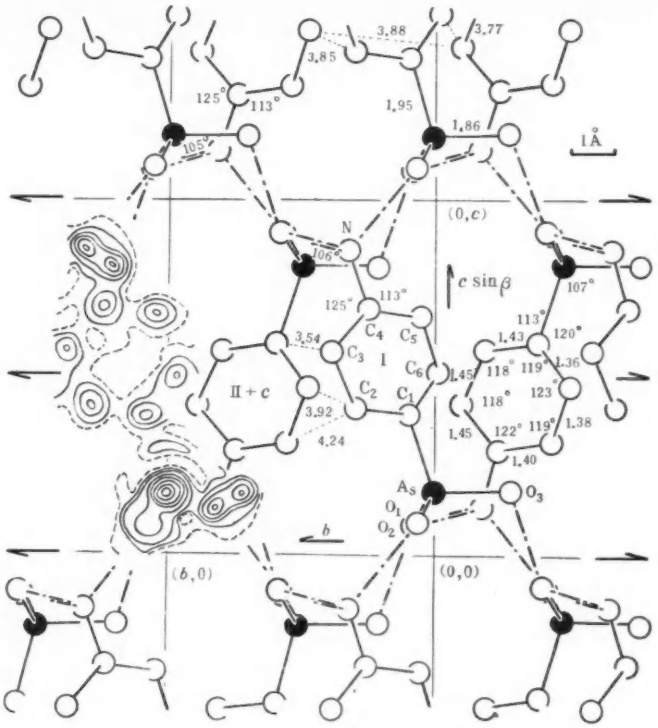



Fig. 3. The structure and the electron-density projection along the a axis, with bond angles, intra- and intermolecular distances (Å). Contours at intervals of $2\,e\,Å^{-2}$, starting at $2\,e\,Å^{-2}$ (broken lines), except the vicinity of the arsenic atom, where contours above $6\,e\,Å^{-2}$ are at intervals of $10\,e\,Å^{-2}$. Dot-dash lines indicate hydrogen bonds.

Table I. Atomic coordinates

| Atom | $x/a$ | $y/b$ | $z/c$ |
|---|---|---|---|
| As | 0.163 | 0 | 0.183 |
| $O_1$ | 0.338 | 0.063 | 0.093 |
| $O_2$ | −0.041 | 0.078 | 0.086 |
| $O_3$ | 0.156 | −0.293 | 0.185 |
| $C_1$ | 0.213 | 0.093 | 0.398 |
| $C_2$ | 0.299 | 0.295 | 0.418 |
| $C_3$ | 0.331 | 0.386 | 0.572 |
| $C_4$ | 0.298 | 0.254 | 0.698 |
| $C_5$ | 0.234 | 0.047 | 0.675 |
| $C_6$ | 0.184 | −0.028 | 0.523 |
| N | 0.327 | 0.318 | 0.863 |

atom, of "valence states" for carbon atom and of $1/3(f_{\parallel}+2f_{\perp})$ for oxygen atom were used, while the scattering curve given by Berghuis et al.[4] was used for arsenic atom. An isotropic temperature factor was estimated to be $2.7\,Å^2$ for all atoms. $R$ indicates for the final coordinates were 13.0 and 14.9% for $(h0l)$ and $(0kl)$ respectively, excluding terms too weak to be observed. The comparison of observed structure factors with calculated ones is shown in Fig. 4.

4) J. Berghuis, I. M. Haanappel, M. Poters, B. O. Loopstra, C. H. MacGillavry and A. L. Veenendaal, ibid., 8, 478 (1955).

### Description of the Structure

The general nature of the structure is shown in Figs. 2 and 3, which are b and a axis projections for this crystal. The arsenic atom is surrounded by a group consisting of three oxygen atoms, $O_1$, $O_2$ and $O_3$ of the arsonic acid and one carbon atom $C_1$ of the benzene ring. The average As–O distance is 1.73 Å, and the As–C distance is 1.95 Å. The disposition of bonds from the arsenic atom appears to be nearly tetrahedral, the angles between the bonds being abnut 109°. The benzene ring is planar and the average distance between adjacent carbon atoms is 1.41 Å, individual values ranging from 1.36 to 1.45 Å. The N–C distance is 1.49 Å and the nitrogen atom is found to lie on the plane of a benzene ring

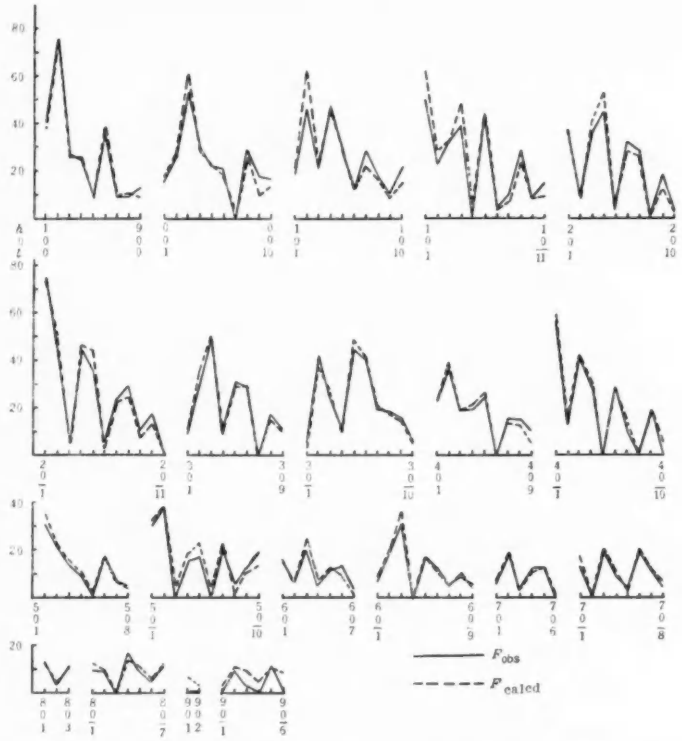



Fig. 4. (a) Comparison of observed and calculated structure factors, F($h0l$).

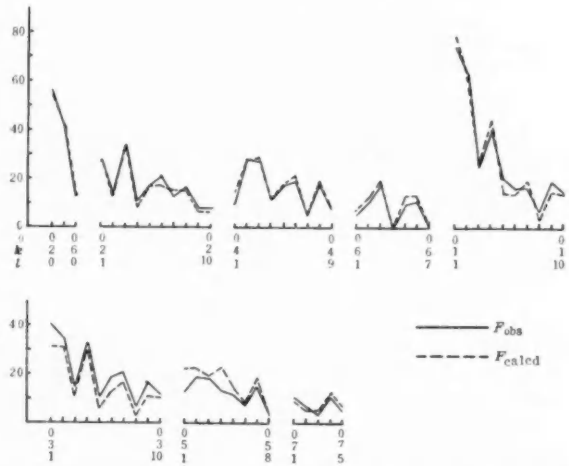



Fig. 4. (b) Comparison of observed and calculated structure factors, F($0kl$).

within the limit of experimental error.

The molecules are held together by a beautiful network of hydrogen bonds. These are four hydrogen atoms available for hydrogen bonding in an asymmetric unit. Two of them come from the *p*-amino group, two come from the arsonic group. There is one hydrogen bond between oxygen atoms and there are three hydrogen bonds between oxygen and nitrogen atoms. The hydrogen bond, with a length 2.52 Å from the atom $O_2$ of molecule I to the atom $O_3$ of molecule II, links molecules with each other to form endless chains along the screw axis perpendicular to the (010) plane. The nitrogen atom in the *p*-amino group of the molecule I forms three hydrogen bonds, the first with a length 2.84 Å to the atom $O_2$ of the molecule $II+c$ (molecule displaced by the unit vector *c*), the second with a length 2.58 Å to the atom $O_1$ of the molecule $I+c$, and the third with a length 2.87 Å to the atom $O_1$ of the molecule $II+a+c$. These three hydrogen bonds connect the endless chains through benzene rings to form a three dimensional net work. This triple hydrogen-bond formation of a nitrogen atom will suggest that one of hydrogen atoms is transferred from an arsonic acid group to the *p*-amino group. On this basis, the formula of the molecule should be written as $NH_3^+ \cdot C_6H_4 \cdot AsO_2(OH)^-$, which indicates that the molecule is in the zwitterion form in the crystal. This conclusion will be supported by the fact that this acid is strictly monobasic[5].

There is no seriously short van der Waals contact in this structure. The shortest distance between nighboring molecules, 3.51 Å, is found between the atom $O_2$ of the molecule I and the arsenic atom of the molecule II. There is also a contact at 3.54 Å between the atom $O_1$ of the molecule I and the atom $C_1$ of the molecule $II+a+c-b$. The shortest contact between adjacent benzene rings occurs at 3.54 Å between the atom $C_1'$ of the molecule I and the atom $C_3$ of the molecule $II+a+c-b$. Other intermolecular distances exceed 3.55 Å. A comparison of this structure with that of the benzenearsonic acid is interesting. They are closely similar in having endless chains formed by the hydrogen bonds between arsonic acid groups, while in *p*-aminobenzenearsonic acid there are additional hydrogen bonds to connect these chains. This difference in mode of packing will explain why the crystal of *p*-aminobenzenearsonic acid has no cleavage, in contrast to that of benzenearsonic acid which shows cleavages along endless chains.

The author wishs to express his sincere thanks to Professor I. Nitta and Professor T. Watanabé of Osaka University for their helpful advice, and to Professor H. Nakata of Konan University for supplying the specimens.

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5) A. E. Goddard, "A Text-book of Inorganic Chemistry", Vol. XI., Part II, Charles Griffin and Co., London (1930), p. 179.

# *Mass Spectrometric Study on Adsorption of Water Vapor on a Graphite Surface*

By Hokotomo Inouye

(Received September 17, 1959)

Although it is of interest in connection with the study of the adsorption of gas on a solid surface to know what sorts of ions are formed by electron bombardment at the surface, there are few mass spectrometric studies on the subject.

By electron bombardment at surface, ions are formed both on the surface and in the gas phase. Therefore, it is important to distinguish the ions which are formed from adsorbed molecules on the surface from those formed simultaneously in the space adjacent to the surface. For this purpose the author has devised a method to know places of formation of ions by analyzing their peak shapes obtained by means of a single focusing mass spectrometer with a modified ionization chamber.

Plumlee and Smith[1] found that $O^+$ was

1) R. H. Plumlee and L. P. Smith, *J. Appl. Phys.*, **21**, 811 (1950).

emitted from an electron-bombarded molybdenum surface by means of a mass spectrometer with the ionization chamber of special structure. However, the author's method may be simpler and give more precise results than Plumlee's method.

The results obtained by application of the author's method to the ions formed by electron bombardment at a graphite surface covered with adsorbed water vapor are described below.

## Experimental

In Fig. 1 is shown the schematic diagram of the mass spectrometer used in the present work. The

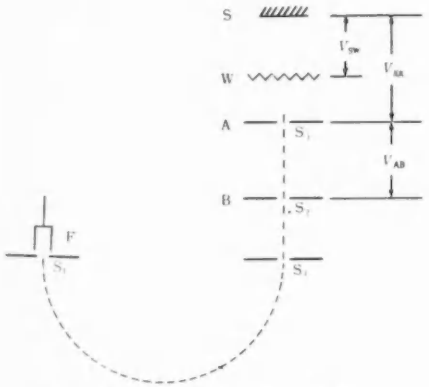


Fig. 1. Schematic diagram of the mass spectrometer.

repeller is replaced by a solid surface, S, to be studied. A hot filament, W, for an electron source is placed between S and the drawing-out electrode, A. Thermoelectrons emitted from W are accelerated by a potential difference $V_{SW}$ and strike S, forming ions on the surface and also in the space between the surface and the place where the potential corresponds to the ionization potential of a gas molecule. A part of these ions is drawn out of the slit $S_1$ of A by a definite potential difference $V_{SA}$ and is accelerated by the variable potential difference $V_{AB}$ for voltage scanning. Ions formed at different places in the ionization chamber, even if they have the same $m/e$, acquire different energies from $V_{SA}$, and hence, for scanning all of them, $V_{AB}$ should be varied over a certain range. Thus the peak shape of the ions will be determined by their distribution in the ionization chamber.

**Peak Shape of the Ions Formed on the Surface.**—If all the ions of one kind are emitted from the surface with zero initial kinetic energy, the only value, ${}_sV_{AB}$, of $V_{AB}$ will be sufficient to bring the ions to the exit slit, $S_4$, of the analyzer. The peak shape will be a symmetrical one characteristic of the instrument (Peak 1). Now, let $V_s$ be the total accelerating potential ($V_{SA}+{}_sV_{AB}$) for the apex of this peak.

If the ion has a certain initial kinetic energy $V_0$ and the angle between its direction and the normal to the surface is $\theta$, $V_{AB}$ bringing the ion to $S_4$ is ${}_sV_{AB}-V_0\cos\theta$, since it has the energy of $V_{SA}-V_0\cos\theta$ at $S_1$. As the directional divergency of the ion beam at $S_2$ is small owing to the geometry of the instrument, the position of the peak apex can be determined only by the energy divergency, or the distribution of $\theta$, among the ions passing through $S_3$. Some ions formed even with great values of $\theta$ are able to enter the analyzer through $S_3$. The value of $\theta$ of the most abundant ions in this distribution is assumed to be $\theta_m$. Then the peak apex will move from $V_s$ by $V_0\cos\theta_m$ towards the lower potential side on the potential axis representing $V_{SA}+V_{AB}$. The peak shape also depends on the directional distribution of the ions at formation and on the geometry of the instrument. Generally, the peak width is broader than that of the ions with zero initial kinetic energy (Peak 2).

If the magnitude of the initial kinetic energy extends over a certain range, this distribution will also affect the position and shape of the peak.

**Peak Shape of the Ions Formed in the Gas Phase.**—If the energy of an electron emitted from W becomes equal to the ionization potential $J$ of a gas molecule at P on the way to S, the molecule in the space between P and S will be ionized by a collision with the electron. The number of ions formed per unit volume, the unit electronic current and the unit time is given by the product of the ionization probability and the density of the gas molecules. Ionization probability increases with the increasing energy of the incident electron and decreases after reaching the maximum. Therefore, the number of the ions formed along the electron path increases from zero at P up to the maximum at S, provided that the applied accelerating potential $V_{SW}$ of the electron is higher than $J$ and lower than the value corresponding to the maximum probability.

Even if the ions thus formed are supposed to have zero initial kinetic energy, they acquire different energies from $V_{SA}$ according to the places of their formation; thus, a wide range of $V_{AB}$ is necessary for scanning all of them. When $V_{AB}$ is equal to ${}_sV_{AB}$ the ions formed just before S can arrive at $S_4$, and at greater values of $V_{AB}$ those formed at places distant from S arrive at $S_4$. The amount of the ions formed just before S is maximum, and it decreases as the distance of the place of the

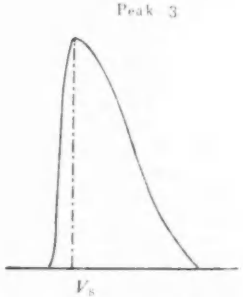


Fig. 2. Peak of the ions formed in the gas phase.

ion formation from S increases. Therefore, the peak has its apex at $V_S$, and its slope at the higher potential side is more gentle than that at the lower potential side as shown in Fig. 2 (Peak 3).

If $V_{SW}$ is higher than the value corresponding to the maximum probability, the place of the maximum ion formation moves from the surface toward P. So the apex moves from $V_S$ toward the higher potential side (Peak 4 in Fig. 3).

If the ions have some initial energies, the peak will be broadened also toward the lower potential side similarly to Peak 2, provided that any ion striking upon the surface underwent an elastic reflection. It may, however, be difficult to distinguish this peak from Peak 3.

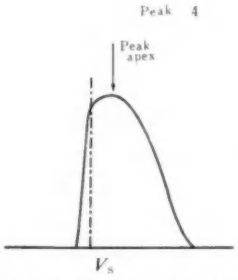


Fig. 3. Peak of the ions formed in the gas phase at $V_{SW}$ exceeding the value corresponding to the maximum ionization probability.

**Peaks of the Ions Formed Both on the Surface and in the Gas Phase.**—If an adsorbed gas is ionized in the gas phase after desorption as neutral molecules or atoms, the peak of the ions will have a shape quite similar to Peak 3. However, it is able to be distimguished from the peak of the ions due to the molecules originally present in the gas phase, because for the former peak the height is proportional to the square of the electronic current but for the latter it is directly proportional to the electronic current[2].

If the adsorbed gas is removed not only directly as ions from the surface but also as neutral molecules or atoms giving the ions of the same $m/e$ afterwards, two kinds of peaks will result either from superposition of Peaks 1 and 3, or from that of Peaks 2 and 3.

(A) All the ions of the same $m/e$ formed on the surface and in the gas phase are supposed to have no initial kinetic energy. Since Peak 1 is obtained for the former and Peak 3 for the latter, the observed peak will be one that results from superposition of both peaks as shown in Fig. 4 (Peak 5).

If $V_{SW}$ higher than the value corresponding to the maximum ionization probability is applied, the observed peak has a shape such as is shown in Fig. 5 (Peak 6), since Peak 4 takes the place of Peak 3 in Fig. 4. Thus, detection of the ions formed on the surface will become easier.

2) Y. Ohta, *J. Chem. Soc. Japan, (Nippon Kwagaku Kwaisi)*, **64**, 849, 986 (1943).

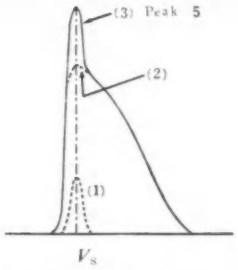


Fig. 4. Peaks of the ions of the same $m/e$ formed simultaneously on the surface and in the gas phase with no initial kinetic energy. (1): peak of the ions formed on the surface, (2): peak of the ions formed in the gas phase, (3): the compounded peak of 1 and 2.

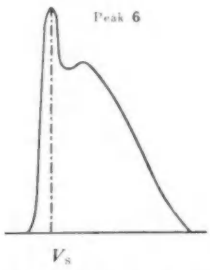


Fig. 5. Peak of the ions of the same $m/e$ formed simultaneously on the surface and in the gas phase by application of $V_{SW}$ higher than the value corresponding to the maximum ionization probability.

(B) If the ions formed on the surface have a fairly high initial kinetic energy but those formed in the gas phase have little, Peak 2 is obtained for the former and Peak 3 for the latter. The compounded peak is such as is shown in Fig. 6 (Peak 7). However, in some cases this peak may be indistinguishable from Peak 2 or Peak 5.

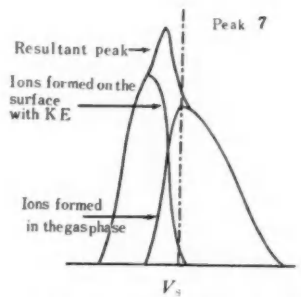


Fig. 6. Peak of the ions formed simultaneously on the surface with an initial kinetic energy and in the gas phase without initial kinetic energy

As described above, the shapes of ion peaks are different from one another according to the places of their formation and to the presence of the initial kinetic energy. From the shape of the peak one may be able to know the place of formation of the ions and also, though not so exactly, to estimate their initial kinetic energy.

## Experimental Results

Ions found in the present work have $m/e$ of 1($H^+$), 2($H_2^+$), 17($HO^+$), 18($H_2O^+$), 28($CO^+$), and 183~186. The peaks of these ions are shown in Figs. 7—12. Besides them a group of ions which is supposed to be formed from grease vapor is found.

1) **$H_2O^+$ and $HO^+$.**—As the peak of $H_2O^+$ has a similar shape to Peak 3 in Fig. 2, this ion is supposed to be formed in the gas phase.

The peak shape of $HO^+$ appears to be similar to Peak 7 rather than to Peak 3. Thus, some of them may be formed on the surface with kinetic energy. However, for the present, $HO^+$ is supposed to be formed only from water molecules in the gas phase, owing to the fact that the observed relative intensity of $HO^+$ to $H_2O^+$ is not greatly different from the result, i.e., 1:4 which Tate and others[3] have obtained on water vapor by voltage scanning, and that it is difficult because of their low intensity to judge certainly whether the peak is similar to Peak 7 or not.

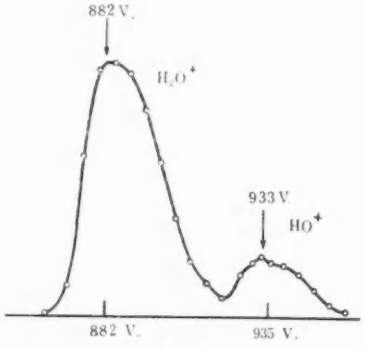


Fig. 7. $H_2O^+$ and $HO^+$. Figures on the potential axis indicate the normal position of the peak apex of the ion.

No measurement has yet been carried out to certify whether these ions are due to residual water vapor or due to the molecules desorbed by electron bombardment.

2) **$H_2^+$.**—As shown in Figs. 8 and 9, the peak shape is similar to Peak 5 in Fig. 4 when $V_{SW}$ is 50 V. and to Peak 6 in Fig. 5 when it is 100 V. The ions are supposed to be formed both on the surface and in the gas phase and neither of them is supposed to have any initial kinetic energy.

3) **$H^+$.**—As the peak has a similar shape, as shown in Fig. 10, to that of Peak 7, the ions are formed both on the surface and in the gas phase, and, at least, those formed on the surface seem to have a certain initial kinetic energy.

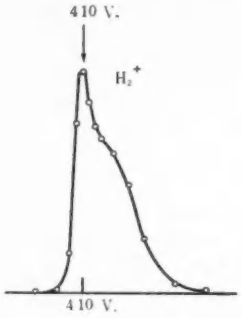


Fig. 8. $H_2^+$ when $V_{SW}$ is 50 V.

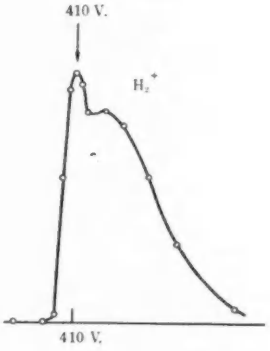


Fig. 9. $H_2^+$ when $V_{SW}$ is 100 V.

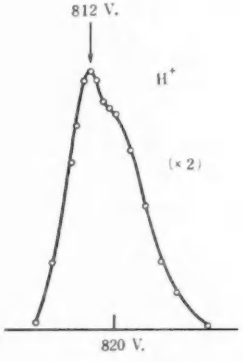


Fig. 10. $H^+$.

3) M. M. Mann, A. Hustrulid and J. T. Tate, *Phys. Rev.*, 58, 340 (1940).

The position of the peak apex of Fig. 8 corresponds to the total accelerating potential of $H_2^+$ leaving the surface without initial kinetic energy. From the value, 410 V., for the apex of $H_2^+$, the position of the apex of $H^+$, peak is calculated to be 820 V., whereas the observed value is 812. Hence, it is shifted by 8 V. towards the lower potential side. This shift will be due to the initial kinetic energy of $H^+$ from the surface.

Now, if the peak of the ions formed in the gas phase is assumed to be curve 1*1 of Fig. 11 and is deducted from the observed curve 3, then curve 2 will result. This curve corresponds to the peak of the ions leaving the surface with initial kinetic energy, the value of which is calculated*2 from the position of the apex to be 10 V.*3

**4) $CO^+$.**—Ions of $m/e$ 28 correspond to $CO^+$ or $N_2^+$, but they are concluded to be $CO^+$ and not $N_2^+$, since $N^+$ ($m/e$ 14) has not been found.

From the peak shape these ions are considered to consist of those formed in the gas phase and of those leaving the surface with kinetic energy, the value of which, however, would be small.

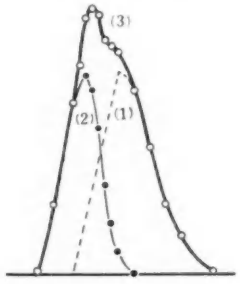


Fig. 11. $H^+$ peak divided into the component peaks.

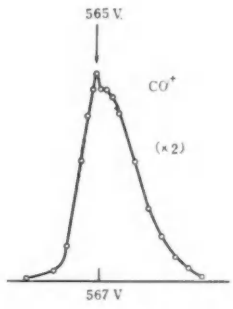


Fig. 12. $CO^+$.

**5) Ions of $m/e$ 183~186.**—The behavior of this group of ions is very different from that of any other ion, and hence they are not supposed to be grease vapor ions but possibly $W^+$ which is produced by electron impact on tungsten vapor evaporating from the heated tungsten filament for the electron source. However, they have not yet been confirmed as such, because the resolving power of the instrument is not sufficient to determine exactly of what $m/e$ of ions they consist.

## Consideration

Despite the fact that hydrogen and carbon monoxide were not introduced into the apparatus on purpose, it was found that $H_2^+$, $H^+$ and $CO^+$ were formed both on the surface and in the gas phase. Therefore, these ions must be formed from the water vapor adsorbed on graphite.

According to the results obtained by the thermal method on adsorption of water vapor on a carbon surface[4,5], $H_2$ will be desorbed from the surface even at room temperatures, and the gas removed from the surface at lower temperatures containing $CO_2$ and a smaller quantity of CO. At higher temperatures CO is increased. These facts are considered to suggest that the reaction of water with carbon gives adsorbed $H_2$ and two types of surface oxides of carbon; one that readily decomposes even by evacuation at room temperatures to give $CO_2$ and the other that is more stable and decomposes at higher temperatures with evolution of CO.

Thus, formation of $H_2^+$ and other ions both on the surface and in the gas phase may be interpreted as follows:

By electron bombardment upon the graphite surface covered with adsorbed water vapor, some of the adsorbed $H_2$ molecules may leave the surface directly as $H_2^+$, and others give $H_2^+$ in the gas phase by successive electron impact after desorption as neutral gaseous molecules. $H_2^+$ formed in the gas phase does not possess initial kinetic energy. Also $H_2^+$ directly leaving the surface will not have initial kinetic energy if the potential curves of the adsorbed $H_2$ molecules are not very different from those of gaseous $H_2$ molecules.

If the more stable surface oxide is assumed to take a configuration such that CO rather

*1 In the curve (1) the peak width due to the instrument is taken into consideration.

*2 As the $\theta$ distribution of the amount of the ions passing through $S_3$ is unknown, the amount of the ions emitted along the axis of the slit system is assumed to be maximum ($\theta_m = 0$).

*3 Several possible peaks were tried as curve (1), but always 10 V. was obtained.

4) R. N. Smith, C. Pierce and C. D. Joel, *J. Phys. Chem.*, **58**, 298 (1954).

5) P. H. Emmett, *Chem. Revs.*, **43**, 69 (1948).

than O is adsorbed on the surface after the apparatus is sufficiently evacuated, it can be removed as CO or $CO^+$ by electron bombardment.

$H^+$ formed in the gas phase may originate from $H_2$ or H leaving the surface by electron bombardment and, in addition, from gaseous water molecules and grease vapor. However, most of them are probably due to dissociative ionization of $H_2$ or ionization of H, since the contribution of $H^+$ from the last two origins to the total $H^+$ current is small.

$H^+$ from the surface may also be due to the adsorbed $H_2$ which resulted from water adsorbed on the graphite surface.

According to the potential curves of higher energy states of $H_2$ molecules, there is the state of unstable $H_2^{2+}$ at 46 V. higher than the normal state, and this $H_2^{2+}$ gives two $H^+$'s, each with kinetic energy of about 7 V., after spontaneous dissociation. Also at 28 V. higher, there is the unstable $^2\Sigma_u$ state of $H_2^+$. It is dissociated into H and $H^+$, each with kinetic energy of about 5 V. Increased energy of the incident electrons can increase this energy up to about 7 V.[6].

If the electronic states of the adsorbed $H_2$ are not greatly different from those of the gaseous molecule, there is sufficient possibility of transition of the adsorbed $H_2$ to unstable $H_2^+$ or $H_2^{2+}$, because the energy $V_{sw}$ of the incident electrons is at least 50 V. When these unstable molecular ions are dissociated, if it is assumed that only one $H^+$ leaves the surface and the other $H^+$ or H is bound to the surface, the leaving $H^+$ will carry all of the initial energy of 10~15 V. for two particles.

Such being the case, and taking into consideration the presence of the directional distribution at formation, the presence of $H^+$ leaving the surface with kinetic energy of about 10 V. will, at least qualitatively, be explainable.

It has also been supposed that some of surface oxides formed from adsorbed water on a graphite surface might have OH-radicals[1]. If that is the case, formation of $HO^+$ on the surface will be possible. However, it was not confirmed in this work as mentioned in Experimental Results 1).

6) H. S. W. Massey and E. H. S. Burhop, "Electronic and Ionic Impact Phenomena", Oxford University Press (1952), p. 231.

## Summary

Peak shapes in mass spectra obtained by voltage scanning using a mass spectrometer with such a modified ionization chamber as that described above are characterized by the places of formation and the initial kinetic energy of the ions. Thus, from the shape of the peak, one may be able to decide the place of formation of the ions and, though not so precisely, to estimate their initial kinetic energy.

When the method was applied to the ions formed by electron bombardment at a graphite surface covered with adsorbed water vapor, it was found that (1) $H_2O^+$ and $HO^+$ were formed from residual or desorbed $H_2O$ only in the gas phase, (2) $H_2^+$, $H^+$ and $CO^+$ were formed both on the surface and in the gas phase, and (3) $H^+$ which formed on the surface had the initial kinetic energy of about 10 V. These results will confirm the fact that the adsorbed water molecule is dissociated into adsorbed $H_2$ and surface oxide of carbon that probably takes a configuration such that CO is adsorbed on the surface.

The author wishes to express his hearty thanks to Professor Nobuji Sasaki of Kyoto University for his guidance throughout the course of this work.

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# *Kolbe's Reaction of Higher Fatty Acids. II. Electrolysis of Lauric Acid by a Pulsating Current with an Artificial Graphite Anode**

By Ryoichi MATSUDA, Takeo HISANO and Daishiro KUBOTA

(Received August 27, 1960)

In the previous paper[1] a study of electrolysis of lauric acid was reported with respect to the relation between the current efficiency of Kolbe's reaction and the anodic current density as well as the alkalinity of the electrolyte, and it was thereby conculded that nickel anode behaved almost similarly to platinum one towards Kolbe's reaction of lauric acid. In connection with the above mentioned result it was undertaken to study behaviors of other anode materials concerning the electrolysis of lauric acid in the present paper.

In Exp. 1 artificial graphite, lead, tantalum, molybdenum, tungsten and iron anodes were employed for electrolysis by direct current, but none of these anodes gave rise to Kolbe's reaction of lauric acid. Accordingly a pulsating current was applied instead of a direct current with the same anodes as those mentioned above, and it was found that only the artificial graphite anode was suitable for Kolbe's reaction. The other anodes were not desirable, being either unable to get the current flow or dissolved partly or entirely in the electrolyte solution. In Exp. 2 the effect of the anodic current density of the pulsating current upon the current efficiency of Kolbe's reaction in the electrolysis with an artificial graphite anode was studied, and comparison was made with the corresponding case employing direct current reported in the previous paper. Exp. 3 dealt with the effect of alkalinity of the electrolyte on the current efficiency of Kolbe's reaction and the result was compared with the corresponding case of the previous paper to discuss the mechanism of Kolbe's reaction.

## Experimental

The electrolytic vessel was the same as described in the previous paper. Four electrolytic solutions were prepared, each of them containing 1 mol. lauric acid and different portion of potassium hydroxide in a mixture of 800 cc. ethanol and 550 cc. water: thus solutions A, B, C and D contained 0.25, 0.5, 0.75 and 1.00 mol. potassium hydroxide respectively and 1 mol. lauric acid. Each electrolysis was conducted with 40 cc. electrolyte at 40°C. In each case 2200 coulombs of either direct or pulsating current were supplied, this quantity of electricity being nearly 90% of that electrochemically equivalent to the lauric acid present in the solution. The pulsating current was generated by a mercury filled Tunger rectifier, and consisted of half-waves of an approximately perfect sinnusoidal curve. The frequency was 60 cycles per second.

## Results and Discussion

**Experiment 1.**—Artificial graphite, lead, tantalum, molybdenum, tungsten and iron were used as anode to investigate the influence of anode material on Kolbe's reaction. The anode was a square plate 1×1 cm. except that of tungsten having a spiral form made of a wire 0.5 mm. of diameter and 15 cm. long. The cathode in each case was a square plate with the effective surface area ten times as large as the anode, and stood face to face with the latter. The anodic current density was 0.4~1.0 amp./cm$^2$. The result is summarised in Tables I and II.

Table I. Behaviors of various anodes in the electrolysis with direct current

| Anode | C | Pb | Ta | Mo | W | Fe |
|---|---|---|---|---|---|---|
| Cathode | C | Pb | Ni | Ni | Ni | Fe |
| Current | none | none | none | flow | flow | flow |
| Kolbe's reaction | none | none | none | none | none | none |

Table II. Behaviors of various anodes in the electrolysis with pulsating current

| Anode | C | Pb | Ta | Mo | W | Fe |
|---|---|---|---|---|---|---|
| Cathode | C | Pb | Ni | Ni | Ni | Fe |
| Current | flow | flow | none | — | flow | flow |
| Kolbe's reaction | partly occurred | none | none | — | none | none |

*Graphite Anode.*—The artificial graphite anode was coupled with a cathode of the same material. When direct current was applied through the circuit, its intensity decreased with unexpected rapidity, e. g., the initial amperage of 80 m amp. decaying to 5 m amp. in ten minutes. No appreciable change of the anode surface was observed during this period. When pulsating current was applied in place of direct current through the electrolyte which had just been treated with the latter, a stationary current was observed at 3 V. A fresh solution was then electrolyzed with pulsating current, and 0.87 g. docosane was obtained with a small amount of alcohol. The content of the vessel after electrolysis was heated with potassium carbonate and filtered. The precipitate was made alkaline with potassium carbonate solution and extracted with ether. The ethereal extract was concentrated and distilled under

* D. Kubota's graduation thesis at Tokushima University.

1) T. Mizuta, T. Hisano and R. Matsuda, This Bulletin, 33, 700 (1960).

reduced pressure, and the resulted 0.75 g. of the fraction with $K_T$=110~130°C was tested by diazo and Bittre color reactions. By both reactions the alcohol was detected. The anode surface was not changed in its appearance by either current. According to Kunugi[2] the use of the artificial graphite anode brought about 11~12% current efficiency of Kolbe's reaction when acetic acid was electrolyzed with direct current.

*Lead Anode.*—Direct current did not flow through the lead anode coupled with a lead cathode, neither changed the surface of the former electrode. However, by applying the pulsating current at 20~23 V., the current of 0.6 amp. was observed to pass, and the anode was entirely dissolved in the electrolyte solution after some thirty minutes.

*Tantalum Anode.*—The tantalum anode was coupled with a nickel cathode. Neither direct nor pulsating current flowed and no apparent change of the anode occurred.

*Molybdenum Anode.*—The molybdenum anode was entirely dissolved in the solution by direct current at 12~13.5 V.

*Tungsten Anode.*—The tungsten anode was coupled with a nickel cathode, and direct current flowed through it, but neither Kolbe's reaction nor any change of the anode occurred. Pulsating current flowed too, but it did not give rise to Kolbe's reaction.

*Iron Anode.*—Both direct and pulsating currents flowed through the iron anode which was coupled with an iron cathode. The anode was partly dissolved in the solution, but no Kolbe's reaction occurred. The reaction is, however, reported[2] to take place to a small extent when acetic acid is electrolyzed with the same anode as above mentioned by direct current.

**Experiment 2.** As the electrolysis by pulsating current with the artificial graphite anode was the only case which was found to be suitable for Kolbe's reaction in Exp. 1, the influence of current density upon the current efficiency was investigated under such condition as mentioned above. As shown in Fig. 1 the increase of current density of the pulsating current favored the current efficiency of Kolbe's reaction. Exp. 2 of the previous paper which dealt with the influenceof current density of direct current upon the current efficiency of Kolbe's reaction showed that there was a similar tendency. In comparing these two cases of electrolysis, however, it is to be born in mind that the solution of the present experiment is more concentrated with respect to potassium hydroxide than the other, and also that higher concentration with respect to the alkali is disadvantageous to the current efficiency of Kolbe's reaction irrespective of the nature of the current. In dealing with the current density of the artificial graphite anode itsporosity has to be taken into consideration.

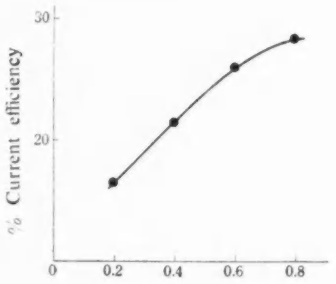


Fig. 1. Influence of anodic current density of pulsating current on docosane production.

**Experiment 3.** The influence of alkalinity of the electrolyte solutions upon Kolbe's reaction with the artificial graphite anode by pulsating current was studied and the result is shown in Fig. 2.

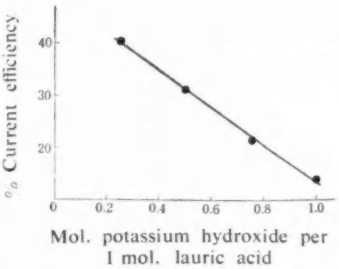


Fig. 2. Influence of alkalinity of solution on docosane production.

Corresponding cases with platinum and nickel anodes by direct current were described in the previous paper. When these two electrolyses are compared with the present case, it is seen that there is a common tendency between them that the current efficiency of Kolbe's reaction decreases linearly with increasing alkalinity. When the alkalinity is the highest one, the current efficiencies of the three cases are close to each other. With the decrease of alkalinity the current efficiency with the artificial graphite anode increases more slowly than the other two. At any rate it is evident that Kolbe's reaction of lauric acid has a close relationship with the alkalinity or the hydrogen ion concentration of the electrolyte solution. Matsuda[3] pointed out that there is an important relationship between Kolbe's reaction and hydrogen ion concentration when the aqueous solution of acetic acid is electrolyzed.

The authors wish to express their thanks to Nippon Oils and Fats Co., Ltd. who kindly offered them the lauric acid.

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2) T. Kunugi, *J. Electrochem. Soc. Japan (Denkikagaku)*, **20**, 208 (1952).

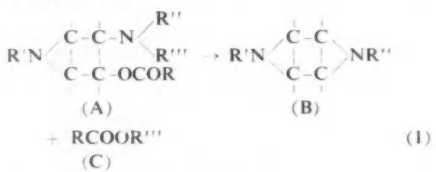
3) B. Matsuda, This Bulletin, **7**, 18, 297 (1932).

# *A New Method for the Preparation of Piperazines. I. Preparation of N-Mono-alkyl(-aryl)-piperazines*

By Kazuo NAKAJIMA

(Received October 8, 1960)

For the preparation of piperazine and its derivatives a number of methods have been proposed up to the present by several investigators[1]. Because of the complexity and the poor yield, these methods still leave much to be desired. Many trials, therefore, have been made by the present author to find out a new convenient route to these compounds. And, after all, it was found that a compound of the general formula A gives a piperazine derivative B under the elimination of an ester C, when it is heated at 200~300°C, according to the following Eq. 1.



(A) (B) (C) (1)

In this equation, R′ and R″ represent alkyl, aralkyl, cycloalkyl, aryl or acyl groups which are destined to remain in the molecule of B after the fission. R‴ also may be an alkyl, aralkyl or cycloalkyl group (equal to or lower than R″), but neither aryl nor acyl group, for these groups are incapable of being removed as a part of the ester C. RCO- in A and in C is an acyl group, but, in fact, it is restricted to the easily available acetyl.

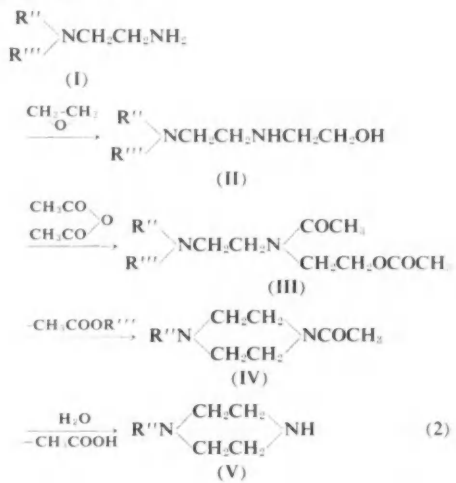
As can be seen from Eq. 1, this reaction seems to be quite a new type of reaction, i.e. the cyclization under the elimination of an ester*.

The actual procedure of this reaction consists in heating the compound A above 200°C, the conditions being arranged so that the ester C can be distilled over as it is formed during the heating, and in fractionating the resulting piperazine B under reduced pressure. Generally speaking from the data of the series of the experiments, the yields are fairly good.

The adequate selections of R′, R″ and R‴ in A make it possible to synthesize various compounds of piperazine-ring system.

As a part of synthetical works in the field of piperazines by the new route, synthesis of *N*-mono-alkyl(-aryl)-piperazines is dealt with in the present paper.

**Synthesis of *N*-Mono-alkyl(-aryl)-piperazines.**—The full course of synthesis of *N*-mono-alkyl-(-aryl)-piperazines (V) from *N*, *N*-disubstituted ethylenediamines (I) is represented by the following Eq. 2.

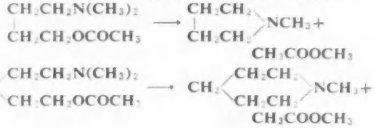


(I) (II) (III) (IV) (V) (2)

*N*, *N*-Disubstituted ethylenediamines (I)[2] are converted into *N*, *N*-disubstituted aminoethyl ethanolamines (II) by the action of ethylene oxide or ethylene chlorohydrin. In this reaction considerable quantities of *N*, *N*-disubstituted aminoethyl diethanolamines are formed, from which II can be isolated by fractionation under

1) D. S. Pratt and C. O. Young, *J. Am. Chem. Soc.*, **40**, 1428 (1918); W. B. Martin and A. E. Martell, ibid., **70**, 1817 (1948); T. S. Moore, H. Boyle and V. M. Thorne, *J. Chem. Soc.*, **1929**, 39; R. Baltzly, J. S. Buck, E. Lorz and W. Schön, *J. Am. Chem. Soc.*, **66**, 263 (1944), K. E. Hamlin et al., ibid., **71**, 2731 (1949); R. Baltzly, ibid., **76**, 1164 (1954); T. Ishiguro, E. Kitamura and M. Matsumura, *J. Pharm. Soc. Japan* (*Yakugaku Zasshi*), **73**, 1110 (1953); **74**, 1162 (1954); **75**, 1370 (1955).

* A similar type of reaction has also been found and will be discussed in detail later in a separate article.



2) K. Nakajima, *J. Chem. Soc. Japan, Pure Chem. Sec.* (*Nippon Kagaku Zasshi*), **81**, 499, 961, 1131, 1477 (1960).

Table I. Properties of $HN<^{CH_2CH_2N(R'')R'''}_{CH_2CH_2OH}$

| Comp. No. | R'' | R''' | Phys. form (color) | M. p. °C | B. p., °C/mmHg† 10 | 20 | 50 | 100 | 760 | N, % Found | Calcd. | Picrate M. p. °C | Platinichloride Dec. p., °C | Pt, % Found | Calcd. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | $CH_3$ | $CH_3$ | Mob. l. (colorless) | | 80 | 97 | 118 | 135 | 205 | 21.02 | 21.19 | 200 (dec.) | 214 | 35.67 | 35.99 |
| 2 | $C_2H_5$ | $C_2H_5$ | 〃 | | 113 | 132 | 152 | 170 | 235 | 17.51 | 17.48 | 90 | * | | |
| 3 | $n$-$C_3H_7$ | $n$-$C_3H_7$ | 〃 | | 134 | 153 | 178 | 199 | 266 | 14.86 | 14.88 | 140 | * | | |
| 4 | $i$-$C_3H_7$ | $i$-$C_3H_7$ | 〃 | | 116 | 135 | 160 | 181 | 248 | 14.77 | 14.88 | 175 | * | | |
| 5 | $n$-$C_4H_9$ | $n$-$C_4H_9$ | Oily l. (colorless) | | 150 | 164 | 188 | 208 | 280 | 13.01 | 12.95 | * | * | | |
| 6 | | $CH_3$ | 〃 | | 168 | 186 | 210 | 230 | 302 | 14.14 | 13.98 | * | * | | |
| 7 | | | 〃 | | 220 | 236 | 264 | 286 (dec.) | | 10.32 | 10.44 | 193 | 212 | 28.78 | 28.76 |
| 8 | | $CH_3$ | 〃 | | 182 | 199 | 222 | 244 | 317 | 14.33 | 14.42 | 153 | * | | |
| 9 | | $C_2H_5$ | Wh. sld. (colorless) | 42 | 192 | 208 | 231 | 252 | 323 | 13.30 | 13.45 | 120 | 195 | 37.40 | 31.56 |

† uncorrected
* not obtained in crystalline form.
Key to abbreviation: Phys.=physical; mob. l.=mobile liquid; wh. sld.=white solid; dec. p.=decomposition point.

Table II. Properties of $CH_3CON<^{CH_2CH_2N(R'')R'''}_{CH_2CH_2OCOCH_3}$

| Comp. No. | R'' | R''' | Phys. form (color) | B. p., °C/mmHg† 6 | 8 | 10 | 20 | 50 | 100 | 760 | N, % Found | Calcd. | Picrate M. p. °C | Platinichloride Dec. p., °C | Pt, % Found | Calcd. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | $CH_3$ | $CH_3$ | Oily l. (colorless) | 140 | 147 | 152 | 170 | 188 | 205 | | 13.05 | 12.95 | 185 | 167 (melt) | 31.01 | 31.17 |
| 2 | $C_2H_5$ | $C_2H_5$ | 〃 | 164 | 174 | 180 | 192 | 212 (dec.) | | | 11.52 | 11.47 | * | * | | |
| 3 | $n$-$C_3H_7$ | $n$-$C_3H_7$ | 〃 | 182 | 189 | 194 | 210 (dec.) | | | | 10.27 | 10.28 | 195 | 198 | | |
| 4 | $i$-$C_3H_7$ | $i$-$C_3H_7$ | 〃 | 170 | 176 | 182 | 194 (dec.) | | | | 10.12 | 10.28 | 220 | * | | |
| 5 | $n$-$C_4H_9$ | $n$-$C_4H_9$ | 〃 | 189 | 296 | 202 | 216 (dec.) | | | | 9.30 | 9.33 | * | 209 | 19.50 | 19.30 |
| 6 | | $CH_3$ | 〃 | 192 | 203 | 210 | 227 (dec.) | | | | 9.89 | 9.90 | * | * | | |
| 7 | | | 〃 | 240 (dec.) | 250 (dec.) | | | | | | 7.75 | 7.95 | * | * | | |
| 8 | | $CH_3$ | 〃 | 211 | 218 | 224 | 243 | 270 | 291 (dec.) | | 10.21 | 10.06 | * | * | | |
| 9 | | $C_2H_5$ | 〃 | 216 | 224 | 232 | 251 | 274 | 295 (dec.) | | 9.51 | 9.58 | * | * | | |

reduced pressure. Some physical properties of II are summarized in Table I.

The second stage is the acetylation of the secondary amino and hydroxyl group in II, which can be effected by two equivalent amounts of acetic anhydride. The reaction proceeds spontaneously with the evolution of heat, and the subsequent distillation under reduced pressure gives III almost in a quantitative yield.

Some physical properties of III are shown in Table II.

On the third stage, III is submitted to the thermal decomposition, which leads to IV and the ester. As outlined in the introduction, distillation of the ester formed during the heating, and subsequent vacuum-fractionation of IV remaining in the flask are the procedures sufficient to give a pure product for the present synthetic purpose.

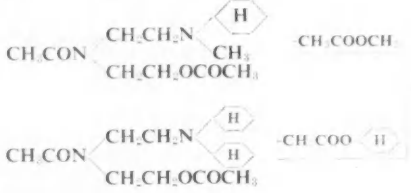
Table III. Properties of $CH_3CON\langle^{CH_2CH_2}_{CH_2CH_2}\rangle NR''$

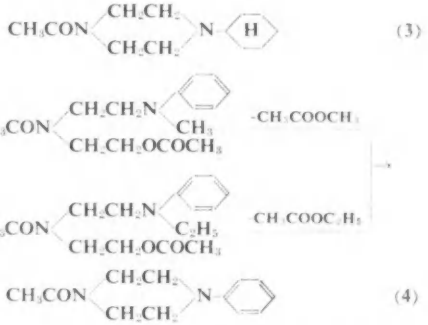
| Comp. No. | R'' | Phys. form (color) | M. p. °C | B. p., °C/mmHg† 10 | 20 | 50 | 100 | 760 | N, % Found | Calcd. | Picrate M. p. °C | Platinichloride Dec. p., °C | Pt, % Found | Calcd. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | $CH_3$ | Mob. l. (colorless) | | | | | | 168 | 19.50 | 19.70 | 280 (dec.) | 270 | 28.02 | 28.10 |
| 2 | $C_2H_5$ | 〃 | | 118 | 138 | 160 | 182 | 254 | 17.93 | 17.93 | 115 | 227 | 27.44 | 27.01 |
| 3 | $n$-$C_3H_7$ | 〃 | | 133 | 151 | 175 | 194 | 265 | 16.30 | 16.45 | 212 (dec.) | * | | |
| 4 | $i$-$C_3H_7$ | 〃 | | 124 | 146 | 171 | 193 | 263 | 16.27 | 16.45 | * | * | | |
| 5 | $n$-$C_4H_9$ | 〃 | | 146 | 165 | 190 | 210 | 280 | 15.11 | 15.20 | 190 (dec.) | * | | |
| 6, 7 | | Oily l. (colorless) | | 186 | 202 | 226 | 248 | 320 | 13.09 | 13.31 | * | * | | |
| 8, 9 | | Cryst. (colorless) | 75 | 206 | 225 | 251 | 270 | 347 | 13.67 | 13.71 | * | 230 | 23.93 | 23.83 |

Table IV. Properties of $HN\langle^{CH_2CH_2}_{CH_2CH_2}\rangle NR''$

| Comp. No. | R'' | Phys. form (color) | B. p., °C/mmHg† 10 | 20 | 50 | 100 | 760 | N, % Found | Calcd. | Picrate M. p. °C | Platinichloride Dec. p., °C | Pt, % Found | Calcd. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | $CH_3$ | Mob. l. (colorless) | | | 44 | 66 | 137 | 28.02 | 27.97 | 270 (dec.) | 275 | 28.11 | 28.25 |
| 2 | $C_2H_5$ | 〃 | | 40 | 64 | 84 | 157 | 24.42 | 24.53 | 250 (dec.) | 280 | 37.34 | 37.23 |
| 3 | $n$-$C_3H_7$ | 〃 | 47 | 65 | 89 | 110 | 180 | 22.00 | 21.85 | 228 | 260 | 36.18 | 36.23 |
| 4 | $i$-$C_3H_7$ | 〃 | 44 | 63 | 87 | 103 | 173 | 21.78 | 21.85 | 240 (dec.) | 266 | 36.24 | 36.23 |
| 5 | $n$-$C_4H_9$ | 〃 | 84 | 101 | 123 | 141 | 208 | 19.43 | 19.70 | 250 (dec.) | 250 | 35.22 | 35.34 |
| 6, 7 | | Oily l. (colorless) | 116 | 135 | 158 | 177 | 248 | 16.45 | 16.65 | 225 (dec.) | 260 | 33.40 | 33.76 |
| 8, 9 | | Oily l. (yellowish) | 139 | 154 | 178 | 180 | 272 | 17.30 | 17.27 | 150 | 259 | 33.99 | 34.10 |

As would be anticipated, β-(*N*-methyl-*N*-cyclohexylaminoethyl)-acetaminoethyl acetate (Table II, No. 6) and β-(*N*, *N*-dicyclohexylaminoethyl)-acetaminoethyl acetate (Table II, No. 7) give the same product, *N*-cyclohexyl-*N'*-acetyl-piperazine (Table III, No. 6, 7) under elimination of methyl acetate or cyclohexyl acetate respectively (Eq. 3). The same applies to the case of β-(*N*-methyl-*N*-phenylaminoethyl)-acetaminoethyl acetate (Table II, No. 8) and β-(*N*-ethyl-*N*-phenylaminoethyl)-acetaminoethyl acetate (Table II, No. 9), *N*-phenyl-*N*-acetyl-piperazine (Table III, No. 8, 9) being equally formed (Eq. 4).





Some physical properties of IV are shown in Table III.

The last stage is the de-acetylation of IV. It may be effected easily by heating the acetyl piperazines with an equal volume of 6 N hydrochloric acid under reflux for 2 hr. The *N*-mono-substituted piperazines thus prepared are a colorless liquid, readily soluble in water

with an exception of *N*-phenyl-piperazine.

Some physical properties of V are cited in Table IV.

The reaction mixture of II and acetic anhydride can conveniently be submitted to the thermal decomposition without isolation of the acetylated compounds.

## Experimental

***N*-(β-Diethylaminoethanol)-aminoethanol (Table I. No. 2).**—Ethylene oxide, generated by dropping 150 g. of 33% sodium hydroxide solution from a pressure-compensated dropping funnel upon a boiling mixture of 100 g. of ethylene chlorohydrin and 50 g. of water under reflux, is passed in a solution of 116 g. (1 mol.) of *N*,*N*-diethylethylenediamine in about 80 g. of methyl alcohol. Contineous shaking and cooling by cold water facilitate the absorption of ethylene oxide in the reaction mixture.

The gain of weight of the reaction mixture will be 44~50 g., and indicates that about one mole of ethylene oxide thereby can be brought into the reaction.

By distillation under atmospheric pressure, about 60 g. of *N*,*N*-diethylethylenediamine (b. p. 150~165°C) is recovered, and by fractionation under reduced pressure, about 50 g. of *N*-β-diethylaminoethylethanolamine, b. p. 113°C/10 mmHg, or 130°C/20 mmHg, and about 40 g. of *N*-β-diethylaminoethyldiethanolamine, b. p. 165°C/10mmHg, or 184°C/20 mmHg are obtained.

Ethylene chlorohydrin may be used instead of ethylene oxide as follows. Forty grams of ethylene chlorohydrin (0.5 mol.) is gradually added from a dropping funnel onto 116 g. (1 mol.) of *N*,*N*-diethylethylenediamine heated under reflux, thereby the reaction proceeds immediately at the rate of addition of the ethylene chlorohydrin. When the addition is complete, the reaction mixture is heated up to 200°C and maintained at this temperature for a while. Owing to the separation of hydrochloride of *N*,*N*-diethylethylenediamine, the reaction mixture is solidified. A hot solution of 30 g. (approx. 0.5 mol.) of potassium hydroxide in 80 cc. of methyl alcohol is gradually added to the reaction mixture with stirring. The precipitate of potassium chloride is removed by filtration and washed with a small quantity of methyl alcohol. After methyl alcohol has been removed from the filtrate and washings, 75 g. of *N*,*N*-diethylethylenediamine is recovered. The residual liquid is submitted to distillation under reduced pressure, whereby 45~50 g. of *N*-β-diethylaminoethylethanolamine and 25~30 g. of *N*-β-diethylaminoethyldiethanolamine are obtained.

***N*-(β-Diethylaminoethyl)-acetaminoethyl Acetate (Table II, No. 2).**—This compound can be obtained by addition of 23 g. (0.22 mol.) of acetic anhydride to 13 g. of *N*-β-diethylaminoethylethanolamine. Acetic acid and an excess of acetic anhydride are distilled off and the residue is distilled under reduced pressure, the expected acetate is collected at 175~177°C/10 mmHg, as a colorless oily liquid —yield 20~21 g. (about 90%).

The practical procedure in this piperazine-synthesis can be carried out so that the reaction mixture of *N*-β-disubstituted-aminoethylethanolamine and acetic anhydride is directly submitted to the thermal decomposition, the isolation of the acetylated compounds being omitted. The techniques here required are quite the same as in use of pure acetates isolated.

***N*-Ethyl-*N'*-acetyl-piperazine (Table III, No. 2).**—Twenty grams of *N*-β-diethylaminoethylacetaminoethyl acetate is heated in a Claisen flask, with a thermometer inserted through the straight neck so deep in the liquid as to read the internal reaction temperature and another thermometer fixed in the side neck of the flask. When the internal temperature reaches up above 250°C, the liquid turns brown in color and the boiling begins with the decomposition into *N*-ethyl-*N'*-acetyl-piperazine and ethyl acetate, which distills over as it is formed.

When the thermal decomposition is complete, the internal temperature is practically settled to a constant, i. e. 250~260°C.

On distillation, pure *N*-ethyl-*N'*-acetyl-piperazine comes over at 252~256°C as a colorless liquid—yield about 7 g. (Ca. 80%).

***N*-Ethyl-piperazine (Table IV, No. 2).**—*N*-Ethyl-*N'*-acetyl-piperazine (5 g.) is heated with 5 cc. of 20% hydrochloric acid under reflux for 2 hr. After the excess of hydrochloric acid has been distilled off, the resulting solution is made alkaline with a sodium hydroxide solution, and extracted with ether in a continuous extractor. The ether layer is dried over anhydrous sodium sulfate, the ether is removed, and the residue is distilled. About 3 g. of pure *N*-ethyl-piperazine is obtained as a colorless liquid b. p. 155~157°C—yield about 90%.

The author wishes to express his sincere gratitude to Professor Ryozo Goto (Kyoto University) for his kind guidance throughout the course of this work.

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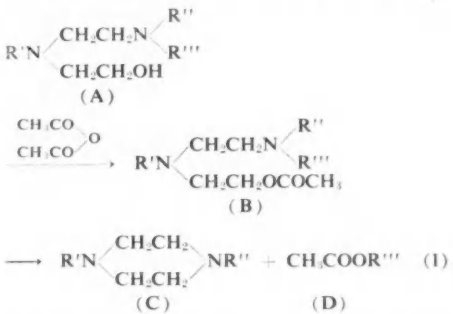
# *A New Method for the Preparation of Piperazines. II. Preparation of N, N'-Disubstituted Piperazines*

By Kazuo NAKAJIMA

(Received September 20, 1960)

A new method for preparing piperazine derivatives has been proposed by the author in the preceding paper[1]. The present paper deals with the preparation of some *N, N'*-disubstituted piperazines by this method. The procedure consists in treating an *N, N', N'*-trisubstituted *N*-$\beta$-aminoethylethanolamine of the general formula A with acetic anhydride to yield an *O*-acetyl derivative B, followed by heating at 200~300°C to split into the desired *N, N'*-disubstituted piperazine C, and an acetic ester D, as is seen in the following Scheme 1;



In the scheme, R' and R'' are alkyl, aralkyl, cycloalkyl or aryl group, whereas R''' is the same group as R'' or a lower alkyl, aralkyl or cycloalkyl group.

If R', R'' and R''' are chosen appropriately, it is possible to synthesize a variety of *N, N'*-disubstituted piperazines.

The properties of *N, N', N'*-trisubstituted *N*-$\beta$-aminoethylethanolamines, which are used as the starting material, of their *O*-acetyl derivatives and of the end-products, *N, N'*-disubstituted piperazines are summarized in Tables I, II and III respectively.

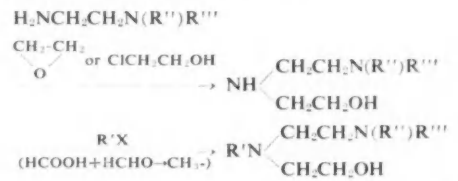
Many proposals have been made hitherto for the preparation of *N, N'*-disubstituted piperazines. Among the compounds of this series listed in Table III, *N, N'*-dimethyl-, *N, N'*-diethyl-, *N, N'*-di-*n*-propyl-, *N*-methyl-*N'*-phenyl, *N*-ethyl-*N'*-phenyl- and *N, N'*-diphenyl-piperazine are known.

The compounds $I_1$*, $I_2$, $I_3$ and $I_4$, where R', R'' and R''' are the same, are easily prepared through alkylation of *N*-$\beta$-aminoethylethanolamine.

The alkylation can be achieved by using alkyl halide, but the methylation is also readily accomplished with formic acid and formalin by the Eschweiler-Clarke procedure.

In the Experimental Part, the synthesis of *N, N', N'*-trimethyl-*N*-$\beta$-aminoethylethanolamine ($I_1$) by the latter procedure and that of *N, N', N'*-tri-*n*-butyl-*N*-$\beta$-aminoethylethanolamine ($I_4$) by the use of *n*-butyl bromide were examplified. The compounds, $I_1$, $I_2$, $I_3$ and $I_4$ are colorless oily liquids, the first two of which are miscible with water and the latter two are sparingly soluble in water.

As expressed in Scheme 2, the compounds $I_5$ to $I_{11}$ were synthesized by the action of ethylene oxide or ethylene chlorohydrin on *N, N'*-disubstituted ethylenediamines, followed by the introduction of R' group.



(2)

The preparation and properties of some of *N*-$\beta$-disubstituted aminoethylethanolamines have been shown in the preceding paper.

In the Experimental Part, the synthesis of ($I_5$) by the Eschweiler-Clarke procedure and that of ($I_{10}$) by the use of an alkyl halide have been illustrated.

The products thus obtained are colorless or yellowish oily liquids, sparingly soluble in water, with the exception of $I_5$ and $I_6$ which are freely soluble.

In compounds $I_{12}$ and $I_{13}$, group R' is cyclohexyl. An attempt was made to introduce this by cyclohexyl bromide, but the formation of a considerable quantity of cyclohexene resulted in a low yield of $I_{12}$ or $I_{13}$. In $I_{14}$ and $I_{15}$, R' is a phenyl group.

$I_{14}$ and $I_{15}$ were therefore prepared from *N*-phenyl-*N*-$\beta$-aminoethylethanolamine.

1) K. Nakajima, This Bulletin, **34**, 651 (1961).

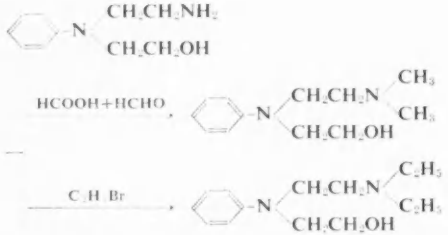
* $I_1$ indicates compound 1 in Table I.

TABLE I. PROPERTIES OF $R'N\langle^{CH_2CH_2N(R'')R'''}_{CH_2CH_2OH}$

| Comp. No. | R' | R'' | R''' | Phys. form (color) | B. p., °C/mmHg 10 | 20 | 50 | 100 | 760 | N, % Found | Calcd. | Picrate M. p. °C | Platinichloride Dec. p. °C | Pt, % Found | Calcd. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | $CH_3$ | $CH_3$ | $CH_3$ | Oily liq. (colorless) | 84 | 100 | 122 | 142 | 206 | 19.15 | 19.16 | 229 (dec.) | 215 | 34.75 | 35.08 |
| 2 | $C_2H_5$ | $C_2H_5$ | $C_2H_5$ | 〃 | 115 | 130 | 154 | 174 | 237 | 15.09 | 14.88 | * | 227 | 32.75 | 32.61 |
| 3 | $n$-$C_3H_7$ | $n$-$C_3H_7$ | $n$-$C_3H_7$ | 〃 | 142 | 157 | 180 | 199 | 266 | 12.30 | 12.16 | 164 | 227 | 30.39 | 30.47 |
| 4 | $n$-$C_4H_9$ | $n$-$C_4H_9$ | $n$-$C_4H_9$ | 〃 | 162 | 180 | 204 | 225 | 295 | 10.31 | 10.28 | * | 220 | 28.35 | 28.59 |
| 5 | $CH_3$ | $C_2H_5$ | $C_2H_5$ | 〃 | 90 | 110 | 134 | 155 | 225～226 | 15.98 | 16.08 | 218 | 215 | 33.39 | 33.40 |
| 6 | $n$-$C_3H_7$ | $C_2H_5$ | $C_2H_5$ | 〃 | 117 | 135 | 159 | 180 | 250 | 13.70 | 13.85 | 163 | 225 | 31.80 | 31.87 |
| 7 | $n$-$C_4H_9$ | $C_2H_5$ | $C_2H_5$ | 〃 | 129 | 158 | 170 | 192 | 262～263 | 12.63 | 12.95 | 66 | 215 | 31.26 | 31.15 |
| 8 | | $C_2H_5$ | $C_2H_5$ | 〃 | 176 | 195 | 220 | 241 | 308 | 11.08 | 11.19 | 98 | 210 | 29.14 | 29.55 |
| 9 | $CH_3$ | $n$-$C_4H_9$ | $n$-$C_4H_9$ | 〃 | 127 | 145 | 169 | 190 | 260 | 12.10 | 12.16 | * | 228 | 30.60 | 30.63 |
| 10 | $C_2H_5$ | | $CH_3$ | Syrupy (colorless) | 179 | 190 | 216 | 235 | 305 | 12.54 | 12.60 | 130 | red. | | |
| 11 | $CH_3$ | | $C_2H_5$ | 〃 | 182 | 200 | 225 | 244 | 315 | 12.60 | 12.60 | * | * | | |
| 12 | | $CH_3$ | $CH_3$ | 〃 | 150 | 165 | 189 | 210 | 280 | 12.97 | 13.07 | 158 | * | | |
| 13 | | $C_2H_5$ | $C_2H_5$ | 〃 | 167 | 185 | 209 | 230 | Ca. 290 (dec.) | 11.21 | 11.56 | * | 190 | 30.10 | 29.91 |
| 14 | | $CH_3$ | $CH_3$ | 〃 | 170 | 195 | 219 | 240 | 310 (dec.) | 13.36 | 13.45 | * | red. | | |
| 15 | | $C_2H_5$ | $C_2H_5$ | 〃 | 180 | 197 | 222 | 242 | 313 (dec.) | 11.60 | 11.85 | 115 | red. | | |
| 16 | | | $-CH_2-CH_2-OH$ | Viscous (colorless) | 264 | 282 | 311 | 330 (dec.) | | 9.24 | 9.33 | 141 | 147 | 27.45 | 27.47 |

* Not obtained in crystalline form.

Key to abbreviation: Phys. form = physical form; liq. = liquid; dec. p. = decomposition point; red. = Platinichloride was reduced; mob. liq. = mobile liquid.



In the Experimental Part, synthesis of *N*-($\beta$-diethylaminoethyl)-*N*-cyclohexylethanolamine ($I_{13}$) is cited.

The next step of this piperazine-synthesis is the formation of *O*-acetyl compounds from the *N*, *N'*, *N'*-trisubstituted *N*-$\beta$-aminoethylethanolamines with acetic anhydride. By the careful fractional distillation of the reaction mixture under reduced pressure the *O*-acetyl derivatives are obtained in an almost theoretical yield. However, the distillation must be carried out under fairly low pressure, say 10 mmHg, in order to obtain the *O*-acetyl compounds in a pure form, because they have a tendency to undergo decomposition over 200°C to piperazine derivatives. For any practical purpose, the *O*-acetyl compounds need not be isolated. The yields of piperazines are 70 to 95 per cent.

In the preparation of the compounds $III_1$ to $III_{15}$ from the corresponding *O*-acetyl compounds, methyl acetate or ethyl acetate is formed. From $II_{16}$, however, ethylene diacetate is formed.

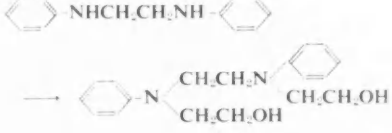
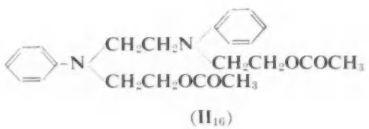
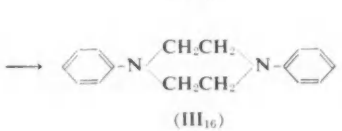


TABLE II. PROPERTIES OF $R'N(CH_2CH_2N(R'')R''')(CH_2CH_2OCOCH_3)$

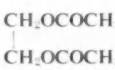
| Comp. No. | R' | R'' | R''' | Phys. form (color) | M. p. °C | B. p., °C/mmHg 10 | 20 | 50 | 100 | 760 | N, % Found | Calcd. | Picrate M. p. °C | Platinichloride Dec. p. °C | Pt, % Found | Calcd. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | $CH_3$ | $CH_3$ | $CH_3$ | Oily liq. (colorless) | | 102 | 119 | 140 | 159 | Ca. 220 (dec.) | 14.58 | 14.88 | 263 | 222 | 32.49 | 32.62 |
| 2 | $C_2H_5$ | $C_2H_5$ | $C_2H_5$ | 〃 | | 125 | 142 | 166 | 186 | Ca. 230 (dec.) | 12.11 | 12.16 | 141 | 224 | 30.35 | 30.47 |
| 3 | $n$-$C_3H_7$ | $n$-$C_3H_7$ | $n$-$C_3H_7$ | 〃 | | 148 | 167 | 191 | 210 | Ca. 256 (dec.) | 10.22 | 10.28 | 134 | 222 | 28.35 | 28.59 |
| 4 | $n$-$C_4H_9$ | $n$-$C_4H_9$ | $n$-$C_4H_9$ | 〃 | | 167 | 185 | 209 | 230 | 229 (dec.) | 8.80 | 8.91 | 125 | 223 | 26.90 | 26.93 |
| 5 | $CH_3$ | $C_2H_5$ | $C_2H_5$ | 〃 | | 104 | 124 | 148 | 170 | 240 (dec.) | 13.10 | 12.95 | 163 | 166 | 31.23 | 31.16 |
| 6 | $n$-$C_3H_7$ | $C_2H_5$ | $C_2H_5$ | 〃 | | 127 | 146 | 169 | 190 (dec.) | | 11.50 | 11.46 | 105 | 208 | 29.70 | 29.82 |
| 7 | $n$-$C_4H_9$ | $C_2H_5$ | $C_2H_5$ | 〃 | | 128 | 157 | 180 | 202 (dec.) | | 10.71 | 10.89 | 125 | 222 | 29.40 | 29.19 |
| 8 | $C_6H_5CH_2$- | $C_2H_5$ | $C_2H_5$ | 〃 | | 180 | 200 | 225 | (dec.) | | 9.32 | 9.58 | 132 | 220 | 27.80 | 27.78 |
| 9 | $CH_3$ | $n$-$C_4H_9$ | $n$-$C_4H_9$ | 〃 | | 156 | 172 | 195 | 216 | (dec.) | 10.11 | 10.23 | 149 | 233 | 28.70 | 28.59 |
| 10 | $C_2H_5$ | $C_6H_5$ | $CH_3$ | Viscous (colorless) | | 196 | 215 (dec.) | | | | 10.59 | 10.60 | 98 | red. | | |
| 11 | $CH_3$ | $C_6H_5$ | $C_2H_5$ | 〃 | | 190 | 210 (dec.) | | | | 11.09 | 10.60 | 132 | 221 | 28.96 | 28.94 |
| 12 | H | $CH_3$ | $CH_3$ | 〃 | | 142 | 160 | 184 | 205 | (dec.) | 10.72 | 10.93 | Ca. 290 | 215 | 29.20 | 29.28 |
| 13 | H | $C_2H_5$ | $C_2H_5$ | 〃 | | 170 | 190 | 214 | 235 (dec.) | | 9.77 | 9.85 | 185 | 210 | 28.01 | 28.11 |
| 14 | $C_6H_5$ | $CH_3$ | $CH_3$ | 〃 | | 195 | 219 | 240 (dec.) | | | 11.36 | 11.19 | * | red. | | |
| 15 | $C_6H_5$ | $C_2H_5$ | $C_2H_5$ | 〃 | | 240 | 250 (dec.) | | | | 10.12 | 10.06 | 160 | 232 | | |
| 16 | $C_6H_5$ | $C_6H_5$ | $-CH_2CH_2OCOCH_3$ | Cryst. (colorless) | 76 | (243/3 mmHg dec.) | | | | | 7.20 | 7.29 | 140 | 202 | 24.80 | 24.56 |

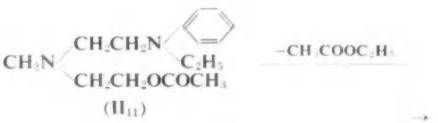


($II_{16}$)

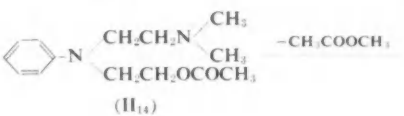


($III_{16}$)

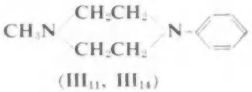




($II_{11}$)



($II_{14}$)



($III_{11}$, $III_{14}$)

$II_{11}$ and $II_{14}$ give the same product with liberation of ethyl acetate and methyl acetate respectively. This is also the case with $II_{10}$ and $II_{15}$.

In the Experimental Part, preparations of *N*, *N'*-dimethylpiperazine ($III_1$), *N*-methyl-*N'*-phenylpiperazine ($III_{11}$), and *N*, *N'*-diphenylpiperazine ($III_{16}$) have been cited.

TABLE III. PROPERTIES OF R'N<$CH_2CH_2$ / $CH_2CH_2$>NR''

| Comp. No. | R' | R'' | Phys. form (color) | M. p. °C | B. p., °C/mmHg 10 | 20 | 50 | 100 | 760 | N, % Found | Calcd. | Picrate M. p. °C | Platinichloride Dec. p. °C | Pt, % Found | Calcd. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | $CH_3$ | $CH_3$ | Mob. liq. (colorless) | | | | 40 | 62 | 132 | 29.51 | 24.53 | 280 (dec.) | Ca. 270 | 37.25 | 37.23 |
| 5 | $CH_3$ | $C_2H_5$ | 〃 | | | 36 | 61 | 82 | 151～153 | 21.70 | 21.85 | 255 (dec.) | 248 | 36.35 | 36.26 |
| 9 | $CH_3$ | $n$-$C_4H_9$ | 〃 | | 62 | 81 | 105 | 126 | 196 | 18.03 | 17.93 | Ca. 240 (dec.) | 280 | 38.45 | 34.46 |
| 12 | $CH_3$ | | Oily liq. (colorless) | | 111 | 131 | 155 | 196 | 246 | 15.42 | 15.37 | 224 (dec.) | 257 | 33.00 | 32.95 |
| {11 {14 | $CH_3$ | | Viscous (yellowish) | 35 | 133 | 150 | 175 | 196 | 266 | 15.80 | 15.90 | Ca. 210 | 245 | 32.99 33.10 | 33.29 |
| 2 | $C_2H_5$ | $C_2H_5$ | Oily liq. (colorless) | | 37 | 56 | 80 | 101 | 171～173 | 19.77 | 19.70 | Ca. 250 (dec.) | 263 | 35.32 | 35.34 |
| 6 | $C_2H_5$ | $n$-$C_3H_7$ | 〃 | | 52 | 76 | 94 | 115 | 188 | 19.82 | 19.93 | 235 | 225 | 34.45 | 34.46 |
| 7 | $C_2H_5$ | $n$-$C_4H_9$ | 〃 | | 76 | 95 | 119 | 140 | 210 | 16.24 | 16.45 | 230 | 260 | 33.50 | 33.63 |
| 8 | $C_2H_5$ | | 〃 | | 150 | 170 | 194 | 208 | 278 | 13.40 | 13.71 | 147 | 260 | 31.63 | 31.77 |
| 13 | $C_2H_5$ | | 〃 | | 134 | 152 | 177 | 197 | 268 | 14.12 | 14.27 | 220 | 258 | 32.03 | 32.18 |
| {10 {15 | $C_2H_5$ | | Viscous (yellowish) | | 150 | 170 | 144 | 215 | 285 | 14.62 | 14.72 | 164 | 245 | 32.52 32.57 | 32.51 |
| 3 | $n$-$C_3H_7$ | $n$-$C_3H_7$ | Oily liq. (colorless) | | 74 | 93 | 117 | 138 | 207～209 | 16.47 | 16.45 | 258 (dec.) | 275 | 33.70 | 33.63 |
| 4 | $n$-$C_4H_9$ | $n$-$C_4H_9$ | 〃 | | 99 | 127 | 152 | 173 | 243 | 14.17 | 14.12 | 245 (dec.) | Ca. 280 | 32.05 | 32.08 |
| 16 |  |  | Cryst. (colorless) | 163 | 226 | 242 | 266 | 288 | (dec.) | 11.75 | 11.76 | 192 | 245 | 30.09 | 30.10 |

## Experimental

**$N,N',N'$-Trimethyl-$N$-$\beta$-aminoethylethanolamine** ($I_1$).—To a mixture of 52 g. (0.5 mol.) of $N$-$\beta$-aminoethylethanolamine and 350 g. of 80% formic acid, heated under reflux, was added 175 g. of formalin (30%) dropwise from a dropping funnel.

A vigorous reaction set in with the evolution of carbon dioxide.

When the addition of formalin was complete, the reaction mixture was boiled under reflux until no more gas was evolved (about 6 hr.). After an addition of 150 ml. of hydrochloric acid (approx. 6 N), the solution was evaporated to dryness under reduced pressure on a steam bath.

To the resulting solid, was added 200 g. of 30% sodium hydroxide solution.

The solution was extracted with ether using a continuous extraction apparatus, until no more volume diminution of the aqueous layer was observed. After the removal of the ether, the residue was distilled fractionally. From the etherial solution there was obtained by the fractinal distillation 58～64 g. of $I_1$, a colorless oily liquid, b. p. 206°C, in an 80% yield.

This compound is readily miscible with water, alcohol, acetone and benzene; $d_4^{20}$ 0.9044. The hydrochloride is colorless crystals, m. p. 187°C.

**$N,N',N'$-Tri-$n$-butyl-$N$-$\beta$-aminoethylethanolamine** ($I_4$).—In a three-necked flask equipped with a reflux condenser, a thermometer and a dropping funnel, was placed 52 g. (0.5 mol.) of $N$-$\beta$-aminoethylethanolamine, and heating was commenced.

When the temperature rose to about 100°C, 37 g. (0.25 mol.) of $n$-butyl bromide was carefully added from the dropping funnel.

When the addition was complete, the temperature of the reaction mixture was raised to about 180°C, and then the mixture was allowed to stand to cool. A hot solution of 14 g. of potassium hydroxide in 30 ml. of methyl alcohol was poured in, shaking well. The crystals of potassium bromide were separated by filtration, and washed with a small amount of methyl alcohol.

From the filtrate methyl alcohol and water were distilled off. The distillation was discontinued when the temperature of the residue in the flask reached 150°C.

This procedure was repeated twice, using 18.5 g. (0.125 mol.) of $n$-butyl bromide and 7 g. (0.125 mol.) of potassium hydroxide in 30 ml. of methyl alcohol the first time, and 10 g. of $n$-butyl bromide and 8 g.

of potassium hydroxide in 20 ml. of methyl alcohol in the second. $I_4$ was purified by distillation under reduced pressure. There was obtained about 110 g. of $I_4$ (approx. 80%) as a colorless oily liquid, b. p. 162°C/10 mmHg or 180°C/20 mmHg.

Almost the same yields were obtained with $I_2$ and $I_3$ in a manner similiar to that described above.

**N-Methyl-N-(β-diethylaminoethyl) ethanolamine** ($I_5$). — Forty grams (0.25 mol.) of *N*-(β-diethylamino-ethyl)ethanolamine was mixed with 40 g. of formic acid (80%). With boiling under reflux, 25 g. of formalin was added dropwise.

The reaction was carried out in the same manner as in $I_1$. The yield of $I_5$, b. p. 225~226°C, was 35 g. (80%).

Similarly, *N*-methyl-*N*-(β-di-*n*-butylaminoethyl)-ethanolamine ($I_9$) could be prepared from *N*-(β-di-*n*-butylaminoethyl)ethanolamine.

**N-Ethyl-N-(β-methylamino-ethyl) ethanolamine** ($I_{10}$). —In a pressure vessel, 22 g. (0.5 mol.) of ethylene oxide dissolved in 50 ml. of methyl alcohol was added to 76 g. (0.5 mol.) of *N*-methyl-*N*-phenyl-ethylenediamine and the mixture was allowed to stand until an exothermal but not violent reaction was complete.

Fractional distillation of this reaction mixture under reduced pressure gave about 30 g. of *N*-(β-methylanilinoethyl)ethanolamine, boiling at 182°C/10 mmHg, 199°C/20 mmHg, or 317°C/760 mmHg. From the fore-run of the distillation, about 20 g. of unchanged starting material, *N*-methyl-*N*-phenyl-ethylenediamine, was recovered (b. p. 124°C/10 mmHg, 142°C/20 mmHg, 257°C/760 mmHg). From the after-run, about 40 g. of *N*-(β-methylanilino-ethyl)-diethanolamine was obtained in the form of colorless oily liquid boiling at 208°C/10 mmHg or 231°C/20 mmHg.

For the purpose of preparing $I_{10}$, a mixture of 19.5 g. (0.1 mol.) of *N*-(β-methylanilino-ethyl)-ethanolamine and 11 g. (0.1 mol.) of ethyl bromide was heated under reflux.

After completion of the vigorous reaction, the reaction mixture was neutralized by adding a sodium hydroxide solution using phenolphthalein as the indicator. The oily layer was separated and distilled under reduced pressure.

There was obtained about 18 g. of $I_{10}$, as a colorless oily liquid boiling at 179°C/10 mmHg or 190°C/20 mmHg in an 80% yield.

**N-(β-Diethylamino-ethyl)-N-cyclohexylethanol-amine** ($I_{13}$). — A mixture of 18 g. (0.1 mol.) of *N*-(β-aminoethyl)-*N*-cyclohexylethanolamine (a colorless oily liquid, b. p. 162°C/10 mmHg, 181°C/20 mmHg, or 295°C/760 mmHg), and 11 g. (0.1 mol.) of ethyl bromide was heated under reflux. After a vigorous reaction had subsided, the cooled reaction mixture was made alkaline with 30% sodium hydroxide solution using phenolphthalein as the indicator.

The oily product that separated was shaken with an equal volume of water**, and distilled fractionally.

About 18 g. of $I_{13}$ was obtained as acolorless oily liquid, boiling at 167°C/10 mmHg or 185°C/20 mmHg.

** There is no appreciable difference between the boiling point of the starting material and that of $I_{13}$. But the former is miscible with water at any proportion, and the latter is sparingly soluble in it. The separation depends upon this difference of solubility.

**N, N'-(Bis-β-hydroxxethyl)-N, N'-diphenyl-ethylenediamine** ($I_{16}$).—To 42 g. (0.2 mol.) of *N,N'*-diphenylethylenediamine was added 18 g. (0.4 mol.) of ethyleneoxide dissolved in 50 ml. of methyl alcohol. After being stored in a refrigerator for two days, the mixture was distilled. At 264°C/10 mmHg or 282°C/20 mmHg. $I_{16}$ was distilled off quantitatively as a colorless and strongly viscous liquid. The melting point of its picrate was 141°C, and that of its platinichloride 147°C.

**N-Methyl-N-(β-dimethylamino-ethyl) aminoethyl Acetate** ($II_1$).—Acetic anhydride (12.5 g.) was added to 14.5 g. (0.1 mol.) of $I_1$. By fractional distillation of the mixture, $II_1$ was obtained at 119°C/20 mmHg, or 140°C/50 mmHg as a colorless oily liquid. The yield was 17 g. (approx. 90%).

**N,N'-Dimethylpiperazine** ($III_1$).—$II_1$ was placed in a Claisen flask equipped with a thermometer inserted through the straight neck to indicate the internal temperature and another thermometer fixed in the side neck to detect the distilling temperature.

Distillation was carefully carried out. At the beginning, the temperature of the content remained at about 206°C, the boiling point of $II_1$. As the decomposition of $II_1$ proceeded, the internal temperature gradually fell, and the distillation of the methyl acetate began. After the theoretical amount of methyl acetate had distilled over, *N,N'*-dimethyl-piperazine was collected at 110~140°C.

Redistillation gave the pure product boiling at 130~132°C. The yield was 90% or greater.

**N-Ethyl-N'-phenylpiperazine** ($III_{15}$).—A reaction mixture of 25 g. (0.1 mol.) of *N*-(β-diethylamino-ethyl)-*N*-phenylethanolamine ($I_{15}$) and 12 g. (0.12 mol.) of acetic anhydride was distilled in the same manner as in the preceding example.

After acetic acid formed and the excess acetic anhydride had distilled out, the temperature of the content increased gradually, reaching 300°C at one time. But as the decomposition proceeded, the internal temperature fell somewhat and ethyl acetate began to distill off at 80~100°C. After completion of the decomposition, the resulting brown liquid was purified by vacuum distillation. This purification furnished about 15 g. of $III_{15}$ in an 80% yield as a yellowish viscous liquid.

**N, N'-Diphenylpiperazine** ($III_{16}$). — Acetic anhydride(25 g.; ca. 0.24 mol.) was added to 30 g. (0.1 mol.) of $I_{16}$. The reaction mixture was submitted to distillation in the same manner as in the preceding example with the object of decomposing it into $III_{16}$ and ethylenediacetate, which distilled out 180~190°C. The residual material was further distilled under reduced pressure. Recrystallization of the solidified distillate from methyl alcohol afforded about 18 g. of $III_{16}$ in colorless crystals, m. p. 163°C. The yield was about 80% of the theory.

The author is deeply grateful to Professor Ryozo Goto, Kyoto University, for giving much helpful advice and encouragement during the course of this work.

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# *Radiation-induced Reaction in an Aqueous Benzoic Acid Solution. I. Dose and Dose Rate Dependencies of Salicylic Acid, and of Biphenyldicarboxylic Acids*

By Akihisa SAKUMOTO and Gen-ichi TSUCHIHASHI

(Received July 28, 1960)

Reactive species such as hydrogen atoms and hydroxyl radicals, and so-called "molecular" products hydrogen and hydrogen peroxide from water are yielded by the actions of ionizing radiation on aqueous solutions. Hydrogen atoms and hydroxyl radicals in these species react rapidly with many solutes dissolved in solutions. The reaction of many organic compounds with these reactive species has been studied by a number of workers.

The radiation-induced reaction of an aqueous benzoic acid solution was studied first by Weiss[1] using X-rays, and recently by Downes[2] using very weak Co 60 gamma rays source. Little attention had been paid by earlier workers to the effect of dissolving oxygen occurring in the reactions when solutions of organic compounds were irradiated by ionizing radiations. The presence of molecular oxygen during irradiation, however, would lead not only to the quantitative differences in the efficiency of the oxidative process but also to some qualitative differences in the reaction products.

In the present work, the radiation-induced reaction of an aqueous benzoic acid solution with, and without, molecular oxygen has been studied and does and dose rate dependencies of the yield of salicylic acid, and of biphenyldicarboxylic acids produced have been examined at high dose and high dose rate, using 10 kc. Co-60 source of the Japan Atomic Energy Research Institute[3].

## Experimental

**Materials.** — Benzoic acid used in this work, obtained from a commercial source, was purified by recrystallization four times from ethanol, m. p. 122°C (uncorrected). Demineralized water was used to prepare a benzoic acid solution. Nitrogen to remove the oxygen contained in sample solutions was purified by letting it bubble through slightly acidified vanadyl sulfate solution[4]. Bomb oxygen was used without further purification.

**Preparation of Solutions.**—Solutions were 0.300% with regard to benzoic acid, and the pH was not specially adjusted. In order to prepare an oxygen free solution, oxygen contained in the solution was driven off by letting purified nitrogen bubble through for two hours. After this treatment, the concentration of oxygen in the solution is estimated to be lower than $1.9\times10^{-5}$ mol./l.[5] Solutions were charged in 30 ml. test tubes, fitted with glass stoppers. The irradiation vessels were cleaned with cleaning solution, rinsed several times, and then washed with distilled water.

Saturation of oxygen during the irradiation was held by continuous bubbling of bomb oxygen in the sample solution. ($[O_2]$ was measured to be $1.2\times10^{-3}$ mol./l.)[5]

**Irradiation.** — Both solutions with and without molecular oxygen were irradiated with gamma rays from 10 kc. Co-60 source with absorbed dose from $6.2\times10^{5}$ to $1.1\times10^{7}$ r and with dose rate from $2.7\times10^{4}$ to $3.9\times10^{5}$ r/hr. at room temperature. Dose rates were measured by means of both ferrous—ferric[6] and ceric-cerous[7] dosimeters, and the amount of energy absorbed in the solutions was calculated using $G$-values of $Fe^{2+}$ oxidized to $Fe^{3+}$ being 15.5 and of $Ce^{4+}$ reduced to $Ce^{3+}$ being 2.45.

**Determination of Salicylic Acid.** — The determination of salicylic acid was carried out by colourimetry. After adjusting the pH of the irradiation solution which, if necessary, was filtered off, between 2.5 and 2.8 by means of 50% acetic acid—3% ammonium acetate buffer, an adequate of 1% ferric chloride solution was added to give salicylic acid complex. The absorbance of salicylic acid complex was measured spectrophotometrically at 530 mμ.

**Determination of Biphenyldicarboxylic Acids.**— Irradiation in the absence of oxygen gave biphenyldicarboxylic acids as precipitate. The precipitate including three isomers of biphenyldicarboxylic acids was separated from the solution using the ultracentrifuge. The collected precipitate was dried for five hours at 80~85°C. Yields of biphenyldicarboxylic acids were determined gravimetrically. Biphenyldicarboxylic acids did not precipitate in the case of irradiation with oxygen.

1) J. Weiss, H. Leobl and G. Stein, *J. Chem. Soc.*, **1951**, 405.
2) A. M. Downes, *Auster. J. Chem.*, **2**, 155 (1958).
3) A. Danno et al., The 7th Hot Laboratories and Equipment Conference, Cleveland (1959), pp. 349~360.
4) L. Meites and J. Meites, *Anal. Chem.*, **20**, 984 (1948).
5) H. Hotta, A. Terakawa and S. Ôno, This Bulletin, **33**, 442 (1960).
6) G. R. A. Johnson and J. Weiss, *Proc. Roy. Soc.*, **A240**, 189 (1957).
7) For example, T. Rigg, G. Stein and J. Weiss, ibid., **A211**, 375 (1952).

## Results and Discussion

Aqueous solutions of benzoic acid were irradiated with Co-60 gamma rays at a fixed absorbed dose of $3.8\times10^{5}$ r by varying dose rate from $2.7\times10^{4}$ to $3.9\times10^{5}$ r/hr. The yield of salcylic acid produced is plotted against the dose rate in Figs. 1 and 2, in which Fig. 1 shows the case of oxygen saturated solutions and Fig. 2 the case of oxygen free solutions. As is shown in these figures, the yield of salicylic acid is decreasing with increasing dose rate in both systems. The yield of salicylic acid in the presence of oxygen was about ten times greater than that in the absence of oxygen.

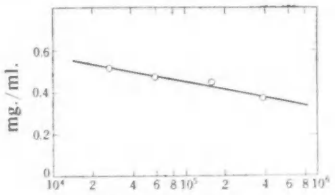



Fig. 1. Yields of salicylic acid produced in oxygen saturated solutions against dose rate. Dose is constant, $3.8\times10^{6}$ r.

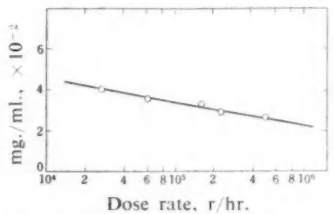



Fig. 2. Yields of salicylic acid produced in oxygen free solutions against dose rate. Dose is constant, $3.8\times10^{6}$ r.

Dose dependence of the yield of salicylic acid by a varying absorbed dose from $6.2\times10^{5}$ to $1.1\times10^{7}$ r at a fixed dose rate of $1.6\times10^{5}$ r/hr. is shown in Figs. 3 and 4, where Fig. 3 shows the system of oxygen saturated and Fig. 4 shows the system of oxygen free solution. Two curves show the same trend that the yield of salicylic acid at high dose is not linearly increasing with the absorbed dose, but gradually increases to approach some constant value. Salicylic acid was produced in both with, and without, molecular oxygen solutions, but biphenyldicarboxylic acids were not observed in the oxygen saturated solutions.

Absorbed dose and dose rate dependencies of yields of biphenyldicarboxylic acids were also studied. Figure 5 shows the plot of yields of biphenyldicarboxylic acids against dose rate.

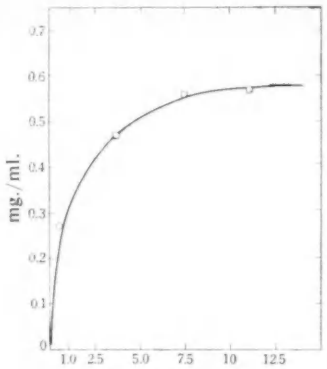



Fig. 3. Yields of salicylic acid produced in oxygen saturated solutions against dose. Dose rate is constant, $1.6\times10^{5}$ r/hr.

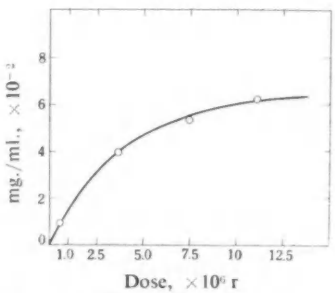



Fig. 4. Yields of salicylic acid produced in oxygen free solutions against dose. Dose rate is constant, $1.6\times10^{5}$ r/hr.

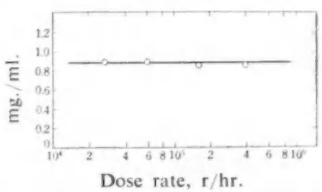



Fig. 5. Yields of biphenyldicarboxylic acid produced in oxygen free solutions against dose rate. Dose is constant, $3.8\times10^{6}$ r.

In this case, the absorbed dose was constant at $3.8\times10^{6}$ r. The yield of the dimer was constant independently of dose rates and $G=$ 0.94 was obtained. Figure 6 shows yields of biphenyldicarboxylic acids against the absorbed dose, which were produced when irradiation was carried out at a fixed dose rate of $1.6\times10^{5}$ r/hr. As is shown in this figure, yields of biphenyldicarboxylic acids have a linear relationship with the absorbed dose. This relationship is quite different from that of the

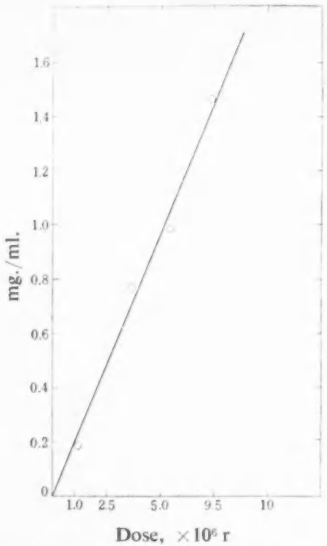



Fig. 6. Yields of biphenyldicarboxylic acid produced in oxygen free solutions against dose. Dose rate is constant, $1.6\times10^5$ r/hr.

yield of salicylic acid as is shown in Figs. 3 and 4.

Basing on the above results, the mechanism of the radiation-induced reaction in an aqueous solution of benzoic acid is assumed as follows.

In the present experiment, the concentration of benzoic acid was 3.0 mg./ml. of solution. At this relatively low concentration, the direct-hit effects of benzoic acid by gamma rays can be neglected. Water is decomposed by ionizing radiation into hydrogen atom, hydroxyl radical, hydrogen peroxide and hydrogen[8].

$$H_2O \rightsquigarrow H\cdot,\ HO\cdot,\ H_2O_2,\ H_2 \qquad (1)$$

Accordingly, the radiation-induced reaction in a dilute aqueous solution is assumed to be initiated by reactive species such as the hydrogen atom and/or the hydroxyl radical produced from the radiolytic decomposition of water.

When water containing molecular oxygen was irradiated, the hydrogen atom produced according to Eq. 1 reacts rapidly with dissolving oxygen giving the hydroperoxy radical[9].

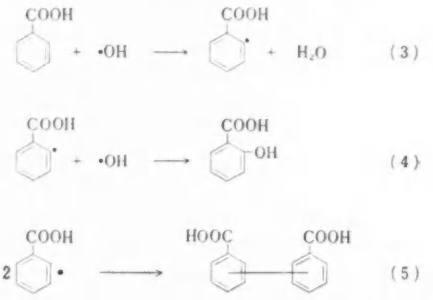
$$H\cdot + O_2 \rightarrow HO_2\cdot \qquad (2)$$

Owing to this reaction, the concentration of hydrogen atom in the presence of oxygen may be considerably lower than that in the absence of oxygen.

If this fact is taken into consideration, radiation-induced reaction in an aqueous solution containing molecular oxygen must be initiated by the hydroxyl radical and or the hydroperoxy radical formed according to Eq. 2. However, it should be noticed that the hydroperoxy radical is assumed to have less oxidizing power than the hydroxyl radical on thermodynamic grounds because the bond dissociation energy of hydrogen peroxide, D(H-O$_2$H), calculated to be 90 kcal./mol., is smaller than that of water, D(H-OH), calculated to be 118 kcal./mol.[10]

Therefore, the hydroperoxy radical appears to be unreactive directly towards benzoic acid. From these reasons, it would be reasonable to consider that the disappearance of benzoic acid in an aqueous solution is initiated by hydrogen-abstraction with the hydroxyl radical produced from radiolytic decomposition of water.

Dehydrogenation of ring hydrogen of benzoic acid, giving hydroxycarbonylphenyl radical as an intermediate, can be followed by a two reaction process: first, the reaction of this radical with hydroxyl radical to form salicylic acid which shows the hydroxylation of ortho-position of benzoic acid, and second, the dimerization of these radicals to produce biphenyldicarboxylic acid as follows.




Biphenyldicarboxylic acids including all kinds of their isomers are insoluble in water giving a pale yellow precipitate and consequently do not suffer from further reaction. The yield of these acids is independent on the dose rate as is shown in Fig. 5, and has a first order relationship with the absorbed dose in the range of the present work (up to $1.1\times10^7$ r) as is shown in Fig. 6. These results signify that the formation of hydroxycarbonylphenyl radical produced as an intermediate according to Eq. 3 is linearly dependent on the absorbed dose.

8) A. O. Allen and H. A. Schwarz, Proceedings of the Second United Nations International Conference on the Peaceful Uses of Atomic Energy, 29, 30 (1958).

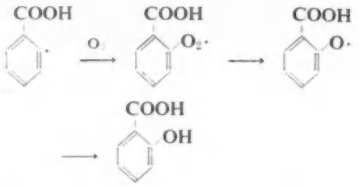
9) P. Riesz and E. J. Hart, *J. Phys. Chem.*, 63, 858 (1959).

10) J. Weiss, *Internat. J. Appl. Radiation Isotopes*, 6, 52 (1959).

Hydroxylation of benzoic acid takes place in all possible positions. Accordingly, three isomers of hydroxybenzoic acid may be formed. In the present work, the yield of only isomer, *o*-hydroxybenzoic acid, i.e. salicylic acid, was determined. The yield of salicylic acid at high dose does not show a linear relationship with absorbed dose, but increases gradually with increasing absorbed dose as is shown in Figs. 3 and 4. On the other hand, it is evident from the experimental results of Weiss[1] that the yield of the acid at the low dose (up to $5\times10^4$ E. U. in his work) has a linear relationship with the absorbed dose. It would seem, therefore, that the trend of the dose-yield curve of salicylic acid at the high dose in the present work may suggest further hydroxylation of salicylic acid to give di-hydroxybenzoic acids and the formation of these acids being more and more remarkable with increasing absorbed dose.

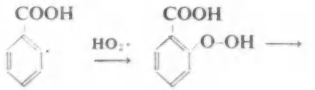
When irradiation of an aqueous solution containing molecular oxygen was carried out, hydroxylation of benzoic acid increased remarkably in comparison with that of the molecular oxygen free solution and the dimerization of hydrocarbonylphenyl radical did not occur. Therefore, the mechanism in this case must be mentioned compared to the different mechanism described above.

If a sufficient amount of molecular oxygen exists in an aqueous solution, it reacts easily with the hydroxycarbonylphenyl radical, as well as the hydrogen, and this reaction results finally in the formation of salicylic acid.




(6)

Consequently, the dimerization of the hydroxycarbonylphenyl radical was suppressed. Concerning the formation of salicylic acid in the presence of molecular oxygen, there is the possibility also of the reaction,




(7)

which can also lead to the eventual formation of salicylic acid. The contribution of this reaction is assumed to be small, because the concentration of oxygen is greater than that of hydroperoxy radical, provided that the reaction rate of the reaction 6 is of the same order as that of 7.

The authors wish to express hearty thanks to Professor Kenjiro Kimura, a director of the Institute, and Dr. A. Danno for their kind encouragement and discussion throughout the entire course of this study.

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# *Radiation-induced Reaction in an Aqueous Benzoic Acid Solution. II. Determination of Products by Isotope Dilution Method*

By Akihisa Sakumoto and Gen-ichi Tsuchihashi

(Received August 3, 1960)

In the preceding paper*, dose and dose rate dependencies of the yield of salicylic acid, and of biphenyldicarboxylic acids were studied in the presence or the absence of molecular oxygen when aqueous solutions of benzoic acid were irradiated with Co-60 gamma rays. In the presence of molecular oxygen, the yield of salicylic acid was greater than that in the absence of molecular oxygen and biphenyldicarboxylic acids was not produced, whereas in the absence of melecular oxygen the main products were biphenyldicarboxylic acids. In the preceding paper, the isomers of hydroxybenzoic and biphenyldicarboxylic acids produced in the solution could not be identified.

The determination of 2-, 3- and 4-hydroxybenzoic acid and biphenyl as reaction products was carried out by Weiss and his collaborators

* Part I: A. Sakumoto and G. Tsuchihashi, This Bulletin, 34, 660 (1961).

using paper chromatography[1]. Recently, Downes separated the isomers of monohydroxybenzoic acids from benzoic acid, and the isomers of dihydroxybenzoic acids from salicylic acid as reaction products by radioactive assay and radiochromatography[2].

In the present work, an isotope dilution method was applied in order to determine the reaction products in the radiolysis of aqueous solutions of benzoic acid (carboxyl-$^{14}$C) in the presence or the absence of molecular oxygen. From the results obtained, a mechanism of the radiation-induced reaction will be discussed.

## Experimental

**Materials.**—Benzoic acid (carboxyl-$^{14}$C) was synthesized from phenylmagnesium bromide and $^{14}CO_2$ by Grignard reaction[3]. This acid was purified by recrystallization from ethanol-water to give a constant specific activity. The specific activity of the acid was $2.289\times10^{-2}$ mc./mol.

Each isomer of biphenyldicarboxylic acid used for the carrier of the isotope dilution method was synthesized according to the method cited in the literatures[4,5]. Each compound was purified by recrystallization except 4,4'-biphenyldicarboxylic acid which was purified by precipitation four times from dilute alkaline solution of it. The melting points** of the isomers were as follows: 2,2'-, 228.0~228.5°C; 3,3'-, 356~357°C. 4,4'-Biphenyldicarboxylic acid did not melt.

Commercial grade 2-, 3-, 4-hydroxybenzoic acid and 2,3-, 2,4-, 2,5-, 2,6-dihydroxybenzoic acid were also purified by recrystallization. The melting points** of the isomers were as follows; 2-, 157~158.5°C; 3-, 200~200.5°C; 4-, 213~213.5°C; 2,3-, 205~206°C; 2,4-, 212.5~213°C; 2,5-, 199~200°C; 2,6-, 149~151°C.

**Preparation of Solution.**—The preparation of 0.300% aqueous benzoic acid (carboxyl-$^{14}$C) solution was carried out by dissolving it in demineralized water. The pH of the solution was not specially adjusted. The irradiation samples of both oxygen free and saturated solution were prepared as described in the preceding paper.

**Irradiations.**—The irradiation vessels and method have been described in the preceding paper. In the present work, irradiations were carried out at the dose rate of $1.6\times10^5$ r/hr. and the absorbed dose of $4.0\times10^6$ r in the presence of molecular oxygen and at the dose rate of $1.7\times10^5$ r/hr. and the absorbed dose of $4.3\times10^6$ r in the absence of molecular oxygen at room temperature. The measurement of the absorbed dose was carried out according to the method as described in Part I.

**Radioactive Assay of Irradiation Products.**—Determination of the yield of irradiation products was carried out as follows. An adequate of analyzing carrier which was weighed accurately was added to an aliquot of irradiated solution, and then dissolved. After the solution was cooled to precipitate the added carrier, the precipitate was filtered off and purified several times by recrystallization to offer a constant counting rate after oxidation to barium carbonate.

Purification of 4,4'-biphenyldicarboxylic acid, being insoluble in ordinary organic solvents, was carried out by dissolving it in dilute sodium hydroxide and reprecipitating it by adding dilute hydrochloric acid.

The isotope dilution method was also applied in order to determine unreacted benzoic acid (carboxyl-$^{14}$C) left in the solution after irradiation. After the addition of non-active benzoic acid, the purification of the acid was carried out by recrystallization six time from ethanol-water and then by sublimation three or five times.

Each sample purified was oxidized according to the Van Slyke-Folch oxidation method[6]. Carbon dioxide liberated after oxidation of a purified sample was absorbed by 0.74 N sodium hydroxide solution and then precipitated as barium carbonate by adding 17.6% barium chloride-2.5% ammonium chloride solution.

The resulting barium carbonate was filtered off, washed with ethanol and dried. The specific activity of barium carbonate was measured at infinite thickness by a Tracerlab. T. G. C.-14 counter.

## Results

Isomers of hydroxybenzoic acid and biphenyldicarboxylic acid were assayed as products when

TABLE I. YIELDS OF PRODUCTS IN OXYGEN FREE SOLUTION OF BENZOIC ACID (CARBOXYL-$^{14}$C) IRRADIATED WITH Co-60 GAMMA RAYS

| Product | Weight mg./ml. | Yield % | *G*-Value |
|---|---|---|---|
| 2-Hydroxybenzoic acid | 0.040 | 1.3 | 0.066 |
| 3-Hydroxybenzoic acid | 0.047 | 1.6 | 0.077 |
| 4-Hydroxybenzoic acid | 0.056 | 1.9 | 0.092 |
| 2,2'-Biphenyldicarboxylic acid | 0.41 | 14 | 0.38 |
| 3,3'-Biphenyldicarboxylic acid | 0.072 | 2.4 | 0.068 |
| 4,4'-Biphenyldicarboxylic acid | 0.30 | 10 | 0.28 |
| Benzoic acid* | 1.86 | 62 | |
| —Benzoic acid** | 1.14 | 38 | 1.88 |

Dose, $4.3\times10^6$ r, dose rate, $1.7\times10^5$ r/hr.
* Unchanged benzoic acid (carboxyl-$^{14}$C) in the irradiated solution.
** The disappearance of benzoic acid (carboxyl-$^{14}$C), calculated from the amount of unchanged benzoic acid (carboxyl-$^{14}$C).

1) J. Weiss, H. Loeble and G. Stein, *J. Chem. Soc.*, **1951**, 405.
2) A. M. Downes, *Austr. J. Chem.*, **2**, 154 (1951).
3) W. G. Dauben and P. E. Yankwich, *Anal. Chem.*, **19**, 828 (1947).
4) "Organic Syntheses", Coll. Vol. I (1948), p. 222.
5) F. Ullman and O. Löwenthal, *Ann.*, **332**, 72 (1904).
** The melting point of each compound is uncorrected.
6) D. D. Van Slyke and H. Folch, *J. Biol. Chem.*, **136**, 509 (1940).

an aqueous solution of benzoic acid (carboxyl-$^{14}$C) irradiated in oxygen free solution. Results obtained are summarized in Table I shown as the yield and *G*-value of each reaction product. In Table I, benzoic acid indicates unchanged benzoic acid (carboxyl-$^{14}$C) which is left in the irradiated solution. *G*-Value of the disappearance of benzoic acid (carboxyl-$^{14}$C) shown as (-benzoic acid) in Table I, calculated from the amount of unchanged benzoic acid (carboxyl-$^{14}$C), is 1.88. The ratio of produced hydroxybenzoic acids and biphenyldicarboxylic acids is approximately 1 : 3. The *G*-value ratio of each hydroxybenzoic acid and each biphenyldicarboxylic acid will be discussed in the following section.

When irradiation was carried out in the presence of oxygen, the yield of products was quantitatively and qualitatively different from those in the absence of oxygen. 2, 3-, 2, 4,- 2, 5- and 2, 6-Dihydroxy benzoic acid are produced in place of isomers of biphenyldicarboxylic acid. The total amount of dihydroxy benzoic acids is 0.31 as *G*-value, being about one fifth of mono-hydroxybenzoic acids. Table II shows the yield and *G*-value of products in the oxygen saturated solution. In this case, *G*-value of 2, 2'-biphenyldicarboxylic acid, the most abundant isomer in the irradiation of oxygen free solution, was estimated to be lower than 0.0003. Therefore, a noticeable amount of isomers of biphenyldicarboxylic acid was not observed in an oxygen saturated solution.

Table II. Yields of products in oxygen saturated solution of benzoic acid (carboxyl-$^{14}$C) irradiated with Co-60 gamma rays

| Product | Weight mg./ml. | Yield % | *G*-value |
|---|---|---|---|
| 2-Hydroxybenzoic acid | 0.45 | 15 | 0.79 |
| 3-Hydroxybenzoic acid | 0.16 | 5.4 | 0.29 |
| 4-Hydroxybenzoic acid | 0.37 | 12 | 0.65 |
| 2,3-Dihydroxy-benzoic acid | 0.072 | 2.4 | 0.12 |
| 2,4-Dihydroxy-benzoic acid | 0.056 | 1.9 | 0.088 |
| 2,5-Dihydroxy-benzoic acid | 0.060 | 2.0 | 0.096 |
| 2,6-Dihydroxy-benzoic acid | 0.0036 | 0.12 | 0.0057 |
| Benzoic acid* | 1.31 | 61 | |
| −Benzoic acid** | 1.19 | 39 | 2.12 |
| 2,2'-Biphenyl-dicarboxylic acid | $2.9\times10^{-4}$ | | 0.0003 |

Dose, $4.0\times10^{6}$ r, dose rate, $1.6\times10^{5}$ r/hr.

* Unchanged benzoic acid (carboxyl-$^{14}$C) in the irradiated solution.

** The disappearance of benzoic acid (carboxyl-$^{14}$C) calculated from the amount of unchanged benzoic acid (carboxyl-$^{14}$C).

## Discussion

The mechanism of radiation-induced reaction of an aqueous solution of organic compound has been studied by a number of workers. The primary process of the reaction is assumed to be radiolytic decomposition of water. Recently, Burton and his collaborators proposed the following *G*-values for the species[7].

$$H_2O \longrightarrow H\cdot,\ HO\cdot,\ H_2,\ H_2O_2 \qquad (1)$$
$$G = 3.70\quad 2.93\quad 0.39\quad 0.78$$

These values will be used in the following discussion.

From the present results of radioactive assay, some information about the initial step of the radiation-induced reaction is obtained. As is shown in Tables I and II, *G*-values of the disappearence of benzoic acid were 2.12 in the presence of molecular oxygen and 1.88 in the absence of molecular oxygen. These values agree fairly well with each other in spite of irradiation conditions being different.

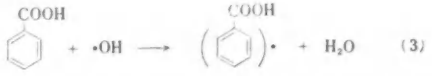
This agreement signifies that dissolving oxygen does not affect the initial step of the decomposition of benzoic acid. It would be, therefore, reasonable to consider that in both cases the initial stage of the reaction is initiated by the attack of the same radical on the benzoic acid molecule.

Hydrogen atom in the reactive species produced from water reacts easily with dissolving oxygen forming hydroperoxy radical in the presence of oxygen.

$$H\cdot + O_2 \rightarrow HO_2\cdot \qquad (2)$$

If the decomposition of benzoic acid is initiated by the hydrogen atom, it is impossible to explain the *G*-value of the decomposition of benzoic acid being almost of the same value regardless of the dissolving of oxygen. Consequently, a hydroxyl radical must be considered to be the only radical which can attack benzoic acid.

Based on the above reasons, the disappearence of benzoic acid in an aqueous solution is considered to be initiated by hydrogen-abstraction of hydroxyl radical as is proposed in the previous paper:



(3)

The concentration of hydroxycarbonylphenyl radical as an intermediate in the reaction must

7) K. C. Kurien, P. V. Phung and M. Burton, *Radiation Research*, **11**, 283 (1959).

TABLE III. *G*-VALUE OF INTERMEDIATE RADICAL

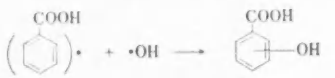
| Condition | Hydroxyl radical: Used for hydrogen-abstraction | Hydroxyl radical: Used for combination with H. C. P. radical | Total | H. C. P. radical*1 |
|---|---|---|---|---|
| Oxygen free | $G(H)$*2 $+2G(B)$*3 $=1.7$ | $G(H)=0.24$ | 1.94 | $G(H)+2G(B)=1.7$ |
| Oxygen saturated | $G(H)+2G(D)$*4 $=2.3$ | zero | 2.3 | $G(H)+G(D)=2.0$ |

*1 H. C. P. radical is hydroxycarbonylphenyl radical
*2 The total *G*-value of hydroxybenzoic acids
*3 The total *G*-value of biphenyldicarboxylic acids
*4 The total *G*-value of dihydroxybenzoic acids
The *G*-value of hydroxyl radical produced in the primary process is 2.92[7].

be of the same value in both cases, because the *G*-value of hydroxyl radical produced primarily from radiolytic decomposition of water is constant of 2.93 regardless of whether with or without oxygen.

In spite of the constant *G*-value of the disappearance of benzoic acid, the products of the reaction in the presence of oxygen were quite different from those in the absence of oxygen. In the former case hydroxybenzoic acids were the predominant products, whereas biphenyldicarboxylic acids were the main products in the latter case.

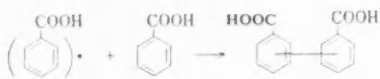
In the absence of oxygen, the total *G*-value of biphenyldicarboxylic acid as main product was 0.73, whereas that of hydroxybenzoic acid was 0.24. Hydroxybenzoic acid may be produced by the combination reaction of hydroxyl radical with hydroxycarbonylphenyl radical:



(4)

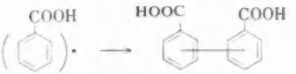
In this case, the amount of hydroxyl radical concerned in the hydroxylation of benzoic acid might be two fold of the amount of hydroxybenzoic acid, and so the *G*-value of this radical participating in the reaction will be calculated to be 0.48, and subsequently, the *G*-value of hydroxycarbonylphenyl radical produced in the reaction as an intermediate might be 0.24.

On the other hand, there are two possibilities of the formation of biphenyldicarboxylic acids from hydroxycarbonylphenyl radical. If biphenyldicarboxylic acids are produced by the substitution reaction of hydroxycarbonylphenyl radical as in the following,



(5)

the disappearance of benzoic acid in this case would be considerably greater than that in the presence of oxygen as mentioned below. It is because the same yield of hydroxycarbonylphenyl radical is proposed in both cases. Accordingly, the formation of biphenyldicarboxylic acids can be attributed to the dimerization of hydroxycarbonylphenyl radical.

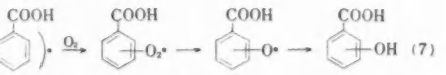


(6)

In this case, the amount of hydroxycarbonylphenyl radical converted into biphenyldicarboxylic acids is two times as much as that of biphenyldicarboxylic acid. If the predominant process of the reaction is the dimerization of hydroxycarbonylphenyl radicals, the total amount of hydroxycarbonylphenyl radical is 1.70 as calculated in Table III.

In the presence of molecular oxygen, hydroxybenzoic acids were predominant products. Noticeable amount of biphenyldicarboxylic acid was not observed. The *G*-value of 2, 2'-biphenyldicarboxylic acid, the most abundant isomer in the absence of molecular oxygen, was reduced to the value of 0.0003. Therefore, it would be unlikely that hydroxybenzoic acid in the presence of molecular oxygen is produced by the combination reaction of hydroxycarbonylphenyl radical with a hydroxyl radical, because the formation of hydroxybenzoic acid by this type of the reaction would be, without fail, accompanying the formation of biphenyldicarboxylic acid as in the case of oxygen free solution.

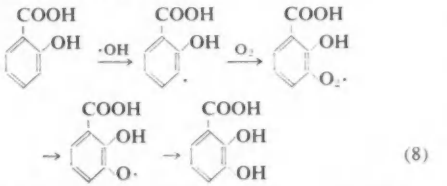
Hydroxycarbonylphenyl radical produced according to Eq. 3 reacts easily with dissolving oxygen to give a hydroxycarbonylphenylperoxy radical. It is, in general, considered that aromatic peroxide is very unstable. Consequently, the peroxy radical would decompose spontaneously into the phenoxy radical and then the reaction results finally in the formation of monohydroxybenzoic acid as is shown in the following:



(7)

The formation of dihydroxybenzoic acids as minor products may be also explained by the

same sequence starting from mono-hydroxybenzoic acid instead of benzoic acid. For example, the following sequence is given for 2, 3-dihydroxybenzoic acid:



(8)

The above mechanism is supported by the radiation-induced reaction of an aqueous ethanol solution by Weiss and collaborators[8]. They found butane-2, 3-diol as main products in the irradiation of an oxygen free solution,

$$CH_3{\cdot}CH_2OH \xrightarrow{HO\cdot} CH_3{\cdot}\dot{C}HOH$$

$$\rightarrow CH_3{\cdot}\underset{OH}{\overset{|}{C}}H{\cdot}\underset{OH}{\overset{|}{C}}H{\cdot}CH_3$$

but, in the presence of oxygen, the dimerization of these radicals was completely suppressed, and acetaldehyde was formed as a predominant product. In this case, they proposed the formation of the peroxy radical ($CH_3{\cdot}\underset{O_2\cdot}{\overset{|}{C}}HOH$) as an intermediate in the reaction.

$$CH_3{\cdot}\dot{C}HOH \xrightarrow{O_2} CH_3{\cdot}\underset{O_2\cdot}{\overset{|}{C}}HOH \rightarrow CH_3CHO$$

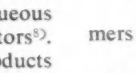
Table III shows the *G*-value of intermediate radicals produced in systems both with and without molecular oxygen. Based on the mechanism given by Eqs. 3, 7 and 8, the *G*-values of hydroxyl and hydroxycarbonylphenyl radicals as an intermediate in the presence of oxygen are calculated to be 2.3 and 2.0, respectively, as is shown in the Table III. The total *G*-value of reacting hydroxyl radical is close to that of hydroxyl radical produced in the primary process (1). Accordingly, it is likely that the most of the hydroxyl radicals formed in the primary process of the reaction react with benzoic acid giving the reaction products. The *G*-value of both hydroxyl and hydroxycarbonylphenyl radicals estimated here are greater in the presence of oxygen than in its absence.

There remain, therefore, some possibilities of the formation of hydroxyl radicals from hydroperoxy radicals produced according to Eq. 2 as follows:

$$2HO_2\cdot \rightarrow H_2O_2 + O_2 \quad (9)$$

$$H_2O_2 \rightarrow 2HO\cdot \quad (10)$$

Some information for the orientation of the hydroxycarbonylphenyl radical is obtained from the experimental values. *G*-Value of 2-, 3- and 4-hydroxycarbonylphenyl radical produced in the absence of oxygen are calculated to be 0.83, 0.21 and 0.65, respectively, basing on the yields of products summerized in Table I. Thus, the *G*-value ratio of 2-: 3-: 4-hyroxycarbonylphenyl radical is 1 : 0.26 : 0.79.

On the other hand, *G*-values of hydroxybenzoic acid, in the presence of oxygen, were 0.79, 0.29 and 0.65 for 2-, 3-, 4-isomer, respectively. In this case, the present authors can not predict any *G*-values of intermediate hydroxy, hydroxycarbonylphenyl radical isomers  produced from mono-hydroxybenzoic acids. If the formation of dihydroxybenzoic acid, being much smaller than that of mono-hydroxybenzoic acid, might be neglected, the *G*-value ratio calculated as 1 : 0.37 : 0.82 for 2-: 3-: 4-hydroxycarbonylphenyl radical in the presence of molecular oxygen agrees fairly well with that in the absence of molecular oxygen. The easiness of the abstraction of ring hydrogen of benzoic acid by hydroxyl radical is shown, basing on the *G*-value ratio of 2-, 3- and 4-hydroxycarbonylphenyl radical, in the following.

ortho > para > meta

It seems also likely that this agreement supports the above postulate that the reaction is initiated by hydrogen-abstraction reaction of hydroxyl radical without regard to dissolving oxygen.

The ratio of hydroxybenzoic acids obtained by Weiss and his collaborators was approximately 5 : 2 : 10 for 2-: 3-: 4-hydroxybenzoic acid in the solution containing molecular oxygen, whereas the ratio was 6 : 4 : 10 under the condition of with insufficient quantity of available oxygen. In their results, the para-isomer was major component[1]. On the other hand, the ratio of mono-hydroxybenzoic acids obtained by Downes was approximately 9 : 5 : 4 for 2-: 3-: 4-hydroxybenzoic acid[2]. In this case, the ortho-isomer was a major component as well as in the present results, although a different ratio was obtained. These different ratios of products may be attributed rather to the different analytical method, the radiation energies or the experimental conditions such as temperature or concentration than to the different dose rate.

We wish to express our thanks to Professor K. Kimura for his kind guidance and Dr. A. Danno for his many helpful discussions.

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*Japan Atomic Energy Research Institute*
*Tokai, Ibaraki-ken*

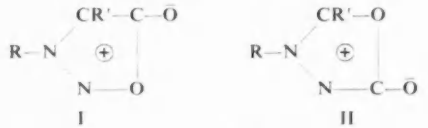
8) G. G. Jayson, G. Scholes and J. Weiss, *J. Chem. Soc.*, 1957, 1358.

# *Studies on Meso-ionic Compounds. XIII*[1]. *ψ-2, 4-Dihydro-4, 5-diphenyl-2-keto-1-oxa-3, 4-diazole**

By Mutsuko HASHIMOTO and Masaki OHTA

(Received October 20, 1960)

Since Earl et al.[2] synthesized in 1935 3-phenylsydnone (I; R=Ph, R'=H), many studies on meso-ionic compounds have been carried out especially with sydnones I, whereas not any meso-ionic compound of type II which differs from the sydnones in the reversal of the –CO·O– grouping is yet known, and we have therefore undertaken a general study of this new meso-ionic system.



VI; R=R'=$C_6H_5$
IX; R=$CH_3$, R'=$C_6H_5$

Fig. 1

Attempts to prepare the compound II were already made by Baker et al.[3] in 1950. Their attempts were mainly based on methods by which the dithio-analogues III had been prepared[4], and the failure of their syntheses was due in several cases to the instability of carbamic acids. On the assumption that iso-cyanate IV might cyclise to the compound II, the reaction of the hydrochloride of *N*-benzoyl-*N*-phenylhydrazine with carbonyl chloride in boiling toluene was also tried, but they obtained *N*, *N'*-di(benzanilido)urea alone.

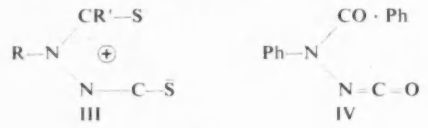
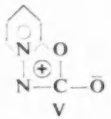


Fig. 2

On the other hand, Hoegerle[5] reported that *N*-aminopyridone-(2) was subjected to the action of carbonyl chloride in chloroform in the presence of potassium carbonate to give the compound V in which the meso-ionic ring in question forms part of a polycyclic system.



V

Fig. 3

Now we treated *N*-benzoyl-*N*-phenylhydrazine with carbonyl chloride under the same conditions as Hoegerle used and recrystallized the product from dry benzene obtaining a crystalline solid $C_{18}H_{16}O_2N_2$, m. p. 161~162°C. This, if formulated as $3 \cdot C_{14}H_{10}O_2N_2$, $C_6H_6$, would correspond to the required meso-ionic compound VI incorporating benzene. Heating the crystalline solid at 100°C under reduced pressure for four days removed benzene from it to afford white crystals, m. p. 165~166°C, which gave analytical figures indicative of the formula $C_{14}H_{10}O_2N_2$.

A comparison of the infrared spectrum of the compound with that of its precursor, *N*-benzoyl-*N*-phenylhydrazine, led us to assign it the structure VI. That is: (1) the disappearance of bands at 3338 and 3278 $cm^{-1}$ in the precursor, arising from NH stretching, (2) the lack of the characteristic band for iso-cyanate group, and (3) the shift of Amide I band in the precursor at 1625 $cm^{-1}$ towards a band at 1755 $cm^{-1}$, which corresponds closely with the ester-carbonyl bands in sydnones listed by Earl et al.[6] and Fugger et al.[7] We therefore designated the compound VI as *ψ*-2, 4-dihydro-4, 5-diphenyl-2-keto-1-oxa-3, 4-diazole following the systematic nomenclature proposed by Baker et al.[8]

The *ψ*-oxadiazole VI is insoluble in absolute ethanol at room temperature, but on heating it converts into ethyl *N*-benzoyl-*N*-phenylhydrazinoformate (VII). When refluxed with cyclohexanol in dry benzene for 6 hr. VI gives

1) Part XII: M. Hashimoto and M. Ohta, This Bulletin, 33, 1394 (1960).

* Presented at the Local Meeting of the Chemical Society of Japan, Hokkaido, July, 1960.

2) J. C. Earl and A. W. Mackney, *J. Chem. Soc.*, **1935**, 899.

3) W. Baker, W. D. Ollis and V. D. Poole, ibid., **1950**, 1547.

4) M. Busch et al., *Ber.*, **28**, 2635 (1895); *J. pr. Chem.*, **60**, 218, 228, 231, 236 (1899); **67**, 201, 202, 246, 250, 257 (1903); W. Baker et al., *J. Chem. Soc.*, **1951**, 289.

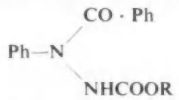
5) K. Hoegerle, *Helv. Chim. Acta*, **41**, 548 (1958).

6) J. C. Earl et al., *J. Chem. Soc.*, **1951**, 2207.

7) J. Fugger et al., *J. Am. Chem. Soc.*, **77**, 1845 (1955).

8) W. Baker, W. D. Ollis and V. D. Poole, *J. Chem. Soc.*, **1949**, 311.

cyclohexyl *N*-benzoyl-*N*-phenylhydrazinoformate (VIII). Heating VI with *N*-benzoyl-*N*-phenylhydrazine at 100°C for 20 min. affords



VII; $R = C_2H_5$
VIII; $R = C_6H_{11}$

Fig. 4

*N*, *N'*-di(benzanilido)urea, which has a lower melting point by 10°C than that reported by Baker et al., but gives the correct analytical values. The same product is also obtained on treatment of VI with boiling water for 3 hr. When heated with aniline at 100°C for 15 min., VI gives 1-benzoyl-1, 4-diphenylsemicarbazide. On treatment with concentrated aqueous ammonia or aqueous dimethylamine, VI gives not the corresponding semicarbazides, but benzamide or *N*-benzoyl-*N*-phenylhydrazine, respectively.

These reactions which suggest the presence of a iso-cyanate group in a molecule were also observed in the polycyclic analogue V[5]. However, the fact that V can be recrystallized from ethanol but VI suffers a ring fission from hot ethanol indicates that VI is less stable than V.

By acid hydrolysis, VI regenerates *N*-benzoyl-*N*-phenylhydrazine. The probable mechanism of the above described hydrolysis is shown in

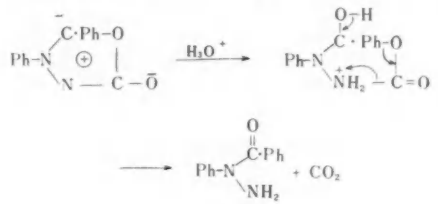


Fig. 5

Fig. 5 after that of acid hydrolysis of sydnones proposed by Baker et al.[9] Unlike sydnones**, *N*-benzoyl-*N*-phenylhydrazine obtained here is unaffected by acid and therefore no further degradation towards phenylhydrazine and benzoic acid might occur.

By alkaline hydrolysis, VI affords phenylhydrazine and benzoic acid. This observation could best be accounted for, if it is considered that the hydrolysis of lactonic group of VI produces unstable intermediate *N'*-carboxy-*N*-benzoyl-*N*-phenylhydrazine and this immediately decomposes to phenylhydrazine and benzoic acid.

Besides the above diphenyl derivative VI, attempts to prepare some analogues were frustrated except $\phi$-2, 4-dihydro-4-methyl-5-phenyl-2-keto-1-oxa-3, 4-diazole (IX) by the inaccessibility of $\alpha$-acylhydrazines. The compound IX was prepared, in very poor yield, by the same treatment of *N*-benzoyl-*N*-methylhydrazine as that used for VI. Recrystallization from dry benzene afforded colorless needles, m. p. 150°C, which gave analytical figures indicative of the formula $C_9H_8O_2N_2$ (IX). Owing to the poor yield both of *N*-benzoyl-*N*-methylhydrazine and of IX, we obtained too small a quantity of IX to examine its infrared spectrum or to perform various reactions similar to those to which diphenyl derivative VI was subjected.

## Experimental

***N*-Benzoyl-*N*-phenylhydrazine.**—A mixture of *N'*-acetyl-*N*-benzoyl-*N*-phenylhydrazine (5 g.), concentrated sulfuric acid (5 ml.), water (25 ml.) and ethanol (35 ml.) was refluxed for 2 hr. Silky needles which separated on cooling were filtered off, suspended in plenty of water and neutralized with sodium carbonate affording colorless prisms (3.1 g.), m. p. 66°C. Recrystallization from dilute ethanol raised m. p. to 78°C (the reported melting point is 69~70°C.[10]).

Found: N, 13.03. Calcd. for $C_{13}H_{12}ON_2$: N, 13.20%.

**$\phi$-2, 4-Dihydro-4, 5-diphenyl-2-keto-1-oxa-3, 4-diazole (VI).**—To a solution of *N*-benzoyl-*N*-phenylhydrazine (2 g.) in chloroform (200 ml.) was added finely powdered, anhydrous potassium carbonate (20 g.) and then a violent stream of carbonyl chloride was introduced with vigorous stirring at −7°C for 10 min. After it has been kept standing overnight, reaction mixture was allowed to reflux for 30 min. and sediments were removed. The filtrate was evaporated and the residue was recrystallized from dry benzene to give colorless lancets (1.71 g.), m. p. 161~162°C, which incorporate benzene.

Found: C, 72.16; H, 4.80; N, 10.98. Calcd. for $C_{45}H_{36}O_6N_6$ ($3 \cdot C_{14}H_{10}O_2N_2 \cdot C_6H_6$): C, 72.72; H, 4.53; N, 10.66%.

When this compound was heated at 100°C under reduced pressure, benzene was removed affording white crystals, m. p. 165~166°C.

Found: C, 70.72; H, 4.52; N, 11.62. Calcd. for $C_{14}H_{10}O_2N_2$: C, 70.58; H, 4.23; N, 11.76%.

**Ethyl *N*-Benzoyl-*N*-phenylhydrazinoformate (VII).**—(a) A solution of VI (0.35 g.) in absolute ethanol (10 ml.) was warmed on a water bath and after 3 hr. evaporated under reduced pressure to give white powder (0.37 g.), m. p. 132°C. Recrystallization from dilute ethanol gave colorless

9) W. Baker and W. D. Ollis, *Quart. Rev.*, **11**, 22 (1957).

** When heated with aqueous acid, the sydnones give *N*-substituted hydrazine, carboxylic acid and carbon dioxide. The interesting production of $\alpha$-acylhydrazine is observed only when 3-phenylsydnone is treated with one molecular proportion of water and hydrogen bromide.

10) O. Widman, *Ber.*, **26**, 947 (1893).

needles, m. p. 135~136°C, undepressed by admixture with the authentic sample prepared by route (b).

Found: C, 67.18; H, 5.92; N, 10.03. Calcd. for $C_{16}H_{16}O_3N_2$: C, 67.59; H, 5.67; N, 9.85%.

(b) To a solution of *N*-benzoyl-*N*-phenylhydrazine in ether was added equimolar ethyl chloroformate and the solid which separated was filtered off and recrystallized from dilute ethanol affording colorless needles, m. p. 136°C (Found: N, 9.95%).

**Cyclohexyl *N*-Benzoyl-*N*-phenylhydrazinoformate (VIII).**—A mixture of VI (0.5 g.), cyclohexanol (1 ml.) and dry benzene (20 ml.) was refluxed for 6 hr., evaporated under reduced pressure and the residue washed with ether and recrystallized twice from dilute dioxane to give colorless needles, m. p. 138~139°C.

Found: N, 8.05. Calcd. for $C_{20}H_{22}O_3N_2$: N, 8.28%.

***N, N'*-Di(benzanilido)urea.**—(a) *N*-Benzoyl-*N*-phenylhydrazine (1 g.) and VI (0.5 g.) were finely powdered, mixed up and kept at 100°C for 20 min. The cooled, hard solid was washed thoroughly with ether and further twice with hot chloroform (yield, 0.82 g.). Recrystallization from pyridine gave a white powder, m. p. 263°C (decomp.) (the reported melting point is 274°C[9]).

Found: C, 72.21; H, 5.33; N, 12.81. Calcd. for $C_{27}H_{22}O_3N_4$: C, 72.00; H, 4.89; N, 12.44%.

(b) VI (0.5 g.) was refluxed with water (20 ml.) with stirring for 3 hr. The precipitate was filtered off, washed with chloroform, dried (0.25 g.) and recrystallized from pyridine giving a white powder, m. p. 263.5°C (decomp.) (Found: C, 71.89; H, 4.93; N, 12.76%).

**1-Benzoyl-1, 4-diphenylsemicarbazide.**—VI (0.5 g.) was dissolved in purified aniline (1 ml.), heated at 100°C for 15 min. and then the solid which deposited was collected, washed with ether (yield, 0.6 g.) and recrystallized from dilute ethanol affording colorless needles, m. p. 210~211°C.

Found: C, 72.27; H, 5.37; N, 12.82. Calcd. for $C_{20}H_{17}O_2N_3$: C, 72.49; H, 5.17; N, 12.68%.

**Reaction of VI with Aqueous Ammonia.**—VI (1 g.) was added to concentrated aqueous ammonia (40 ml.) and stirred vigorously. After 3~4 hr. complete dissolution occurred, a pale orange color developing. After it has been kept standing at room temperature for 2 days, the reaction mixture was evaporated under reduced pressure and the residue with a smell of phenylhydrazine was collected, washed with ether, dried (yield, 0.14 g.) and recrystallized from a little water giving colorless needles, m. p. 126~127°C, undepressed by admixture with authentic benzamide.

Found: N, 11.64. Calcd. for $C_7H_7ON$: N, 11.57%.

**Reaction of VI with Aqueous Dimethylamine.**—VI (0.5 g.) was added to 40% aqueous dimethylamine (10 ml.) and stirred vigorously. After 15 min. complete dissolution occurred, an orange color developing. After it has been kept standing at room temperature for 5 days, the reaction mixture was evaporated under reduced pressure to give the residual oil which solidified on addition of concentrated hydrochloric acid. Recrystallization from ethanol-ether yielded colorless needles, m. p. 192~193°C (decomp.), which showed the positive Beilstein test.

Found: N, 11.46. Calcd. for $C_{13}H_{13}ON_2Cl$: N, 11.27%.

The authentic sample prepared by the action of concentrated hydrochloric acid on *N*-benzoyl-*N*-phenylhydrazine had m. p. 191~193°C (decomp.) (Found: N, 11.12%).

**Acid Hydrolysis.**—When VI (1 g.) was warmed with 10% aqueous hydrochloric acid on a water bath, complete dissolution did not occur but the form of crystallization gradually changed. The precipitate was filtered off, dried (0.66 g.) and recrystallized from water affording colorless needles, m. p. 199°C (decomp.), which showed the positive Beilstein test.

Found: C, 62.60; H, 5.49; N, 10.89. Calcd. for $C_{13}H_{13}ON_2Cl$: C, 62.78; H, 5.23; N, 11.3%.

**Alkaline Hydrolysis.**—VI (1 g.) was readily dissolved in 10% aqueous sodium hydroxide. After 45 min. the solution was acidified to give colorless leaflets (0.39 g.), m. p. 122°C, undepressed by admixture with authentic benzoic acid. The acidic filtrate was neutralized and extracted with ether. The extract was dried with sodium sulfate and evaporated to give an oily product, from which on addition of aqueous oxalic acid the oxalate of phenylhydrazine was obtained.

***φ*-2, 4-Dihydro-4-methyl-5-phenyl-2-keto-1-oxa-3,4-diazole (IX).**—To a solution of *N*-benzoyl-*N*-methylhydrazine (3.5 g.), prepared by Michaelis' method[11], in chloroform (600 ml.) was added finely powdered, anhydrous potassium carbonate (60 g.) and then a violent stream of carbonyl chloride was introduced with vigorous stirring at −5~−8°C for 10 min. After it has been kept standing overnight, the reaction mixture was refluxed for 30 min. and sediments were removed. The filtrate was evaporated to give very viscous oil with a strong smell of benzoyl chloride. Addition of ether afforded a small amount of crystalline solid, which was collected and recrystallized from dry benzene giving colorless needles, m. p. 150°C.

Found: C, 61.55; H, 4.88; N, 16.15. Calcd. for $C_9H_5O_2N_2$: C, 61.36; H, 4.58; N, 15.90%.

We are indebted to Dr. Asaji Kondo for microanalyses and to Dr. Tadashi Sato for infrared spectroscopic work.

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11) A. Michaelis and E. Hadanck, ibid., **41**, 3288 (1908).

# *Bile Acids and Steroids. XXI*[1]. *Studies on the Hog Bile Acids (Part 5)*[1]. *On the Oxidation of Epimeric 3,6-Dihydroxycholanoic Acids with N-Bromosuccinimide*[*1]

By Jun'ichi KAWANAMI

(Received September 30, 1960)

Previously, it was described that α-hyodeoxycholic acid is selectively oxidized at C-3 with *N*-bromosuccinimide (NBS) to give 3-oxo-6α-hydroxy-5β-cholanoic acid[2], whereas it has been reported earlier by Wieland[3] that it was preferentially oxidized at C-6 with chromic acid. From this reverse result, it was of interest to investigate the oxidation of epimeric 3,6-dihydroxy-5β-cholanoic acids with NBS. Oxidation was carried out in both dioxane-water (9:1) and acetone-water (7:3) in order to obtain information depending on polarity of the solvent and with 1 and 2 molar equivalents of NBS respectively in order to obtain information depending on selectivity. As seen in Table I, the order of susceptibility to oxidation obtained from the results was as follows:

$$6\beta > 3\beta \ \& \ 3\alpha > 6\alpha \quad (A/B: \text{cis})$$

The 6β-hydroxyl group was most rapidly oxidized, the 6α-hydroxyl group was not attacked and the ease of oxidation of both the 3β- and the 3α-hydroxyl groups were in between. However, the difference between 3β- and 3α-hydroxyl group was not definable in such an experiment. Although there is a method in which the reagent such as NBS is volumetrically titrated, it is presumed to complicate the results on account of two factors, both a consumption by the substrates and a decomposition by the solvent. Therefore, the author examined the oxidation using the absorption band at 1720 $cm^{-1}$ corresponding to the carbonyl group of the six-membered ketone in the infrared spectrum. This band is so strong that it is useful for determination. Since the reaction itself was assumed to be very complicated as mentioned above, it was most reliable to use the optical densities of the six-membered carbonyl band in the infrared spectrum for this purpose. In this case, as methyl 3-oxo-6α-hydroxy-5β-cholanoate was oily, it was unsuitable for preparing the calibration curve. Consequently, methyl lithocholate[7] and methyl 3β-hydroxy-5β-cholanoate[8] were used as starting materials. Ester is also suitable to avoid the overlap of the acid carbonyl band with the six-membered ketone band in the infrared spectrum. As the six-membered carbonyl band was further somewhat overlapped with that of

Table I. The Position Attacked and the Yield in Each Epimer

| Solvent | Dioxane-Water (9:1) | | Acetone-Water (7:3) | |
|---|---|---|---|---|
| Mol. equiv. of NBS | 1 | 2 | 1 | 2 |
| Reaction time at room temperature (20±2°C) | 1.5 hr. | 1.5 hr. | Overnight | 4 days |
| 3α, 6α | 3(27.2%) | 3(30.1%) | 3(41.7%) | 3(61.8%) |
| 3β, 6α[4] | 3(21.3%) | 3(45.7%) | 3(31%) | 3(62.5%) |
| 3β, 6β[5] | 6(77%) | 6(56.6%) | 6(77.5%) | 6(55%) |
| | | 3,6(14.3%) | | 3,6(19.3%) |
| 3α, 6β[6] | 6(70%) | 6(60%) | 6(70%) | 6(59.4%) |
| | | 3,6(7.5%) | | 3,6(16%) |

*1 The rest is abbreviated as NBS.

1) Part XX: J. Kawanami, This Bulletin, **34**, 509 (1961).

2) K. Takeda and J. Kawanami, *J. Biochem.* (*Japan*), **40**, 477 (1953).

3) H. Wieland and E. Dane, *Z. Physiol. Chem.*, **212**, 41 (1932).

4) β-Hyodeoxycholic acid was prepared from 3-oxo-6α-hydroxy-5β-cholanoic acid according to Moffett method. (R. B. Moffett and W. Hoehn, *J. Am. Chem. Soc.*, **69**, 1995 (1947)).

5) Synthesis of 3β, 6β-dihydroxy-5β-cholanoic acid was described in the preceding part XX.

6) 3α, 6β-Dihydroxy-5β-cholanoic acid was prepared from methyl 3α-acetoxy-6-oxo-5β-cholanoate according to Moffett method. (R. B. Moffett and W. Hoehn, *J. Am. Chem. Soc.*, **68**, 1855 (1946)). This compound was also prepared in good yield by using sodium borohyride in place of Raney nickel.

7) Methyl lithocholate was prepared from cholic acid according to the usual method. (S. Sarel and Y. Yanuka, *J. Org. Chem.*, **24**, 2018 (1959)).

8) Methyl 3β-hydroxy-5β-cholanoate was prepared from both Methyl 3-oxo-cholanoate and Methyl 3α-tosyloxy-5β-cholanoate according to Fieser's and Reindel's method respectively. (F. Reindel and K. Niederlandre, *Ber.*, **68**, 1243 (1935); L. F. Fieser and J. C. Babcock, *J. Am. Chem. Soc.*, **74**, 5474 (1952)).

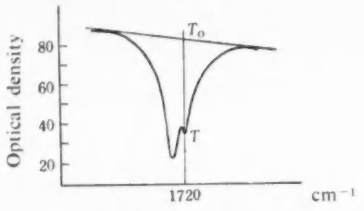



Fig. 1. Baseline method.

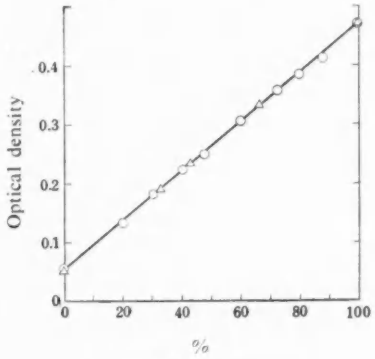



Fig. 2. Calibration curve.
—○— 3$\alpha$-epimer; —△— 3$\beta$-epimer

the ester group, $T_0$ was estimated according to the baseline method (Fig. 1).

The calibration curve was made by using a variety of mixtures consisting of each methyl 3$\beta$- or 3$\alpha$-hydroxy-5$\beta$-cholanoate and methyl 3-oxo-5$\beta$-cholanoate. As shown in Fig. 2, the calibration curve plotting the relationship between the optical density and the concentration ($W/W$%) of the oxidation product, 3-oxo-5$\beta$-cholanoate to each of methyl 3$\beta$- or 3$\alpha$-hydroxy-5$\beta$-cholanoate, formed a straight line which indicated its usefulness for a quantitative analysis. The values thus obtained are shown in Tables II and III. Then, the

TABLE II. RELATIONSHIP BETWEEN OPTICAL DENSITY AND RATIO ($W/W$%) OF THE 3-OXO DERIVATIVE TO THE 3$\alpha$-EPIMER

| Percentage of 3-oxo deriv. | 3-Oxo mg. | 3$\alpha$-OH mg. | $CCl_4$ + Sample mg. | $W$ % | $\overline{T_0}$ | $\overline{T}$ |
|---|---|---|---|---|---|---|
| 0 | 0 | 5.0 | 589.0 | 0.850 | 88.3 | 79.4 |
| 20 | 0.8 | 3.2 | 472.0 | 0.848 | 87.8 | 67.7 |
| 30 | 1.8 | 4.2 | 717.2 | 0.838 | 87.6 | 61.7 |
| 40 | 2.0 | 3.0 | 604.0 | 0.828 | 88.0 | 57.9 |
| 48 | 4.5 | 4.9 | 1163.1 | 0.807 | 87.7 | 55.2 |
| 60 | 3.0 | 2.0 | 594.0 | 0.842 | 87.7 | 48.5 |
| 72 | 4.3 | 1.7 | 704.5 | 0.852 | 87.3 | 43.5 |
| 80 | 4.0 | 1.0 | 588.0 | 0.850 | 87.3 | 41.3 |
| 87.4 | 6.9 | 1.0 | 942.9 | 0.837 | 87.1 | 39.6 |
| 100 | 6.3 | 0 | 792.4 | 0.795 | 87.2 | 36.6 |

TABLE III. RELATIONSHIP BETWEEN OPTICAL DENSITY AND RATIO ($W/W$%) OF THE 3-OXO DERIVATIVE TO THE 3$\beta$-EPIMER

| Percentage of 3-oxo deriv. | 3-Oxo mg. | 3$\beta$-OH mg. | Sample +$CCl_4$ mg. | $W$ % | $\overline{T_0}$ | $\overline{T}$ |
|---|---|---|---|---|---|---|
| 0 | 0 | 7.2 | 897.3 | 0.801 | 87.8 | 80.0 |
| 33.3 | 2.7 | 5.4 | 924.9 | 0.875 | 87.7 | 60.0 |
| 43.4 | 3.7 | 4.9 | 948.9 | 0.908 | 87.4 | 53.6 |
| 66.7 | 6.2 | 3.1 | 1081.8 | 0.859 | 87.1 | 45.5 |
| 100 | 6.3 | 0 | 792.4 | 0.795 | 87.2 | 36.6 |

TABLE IV. RELATIONSHIP BETWEEN THE YIELD OF OXIDATION PRODUCTS AND TIME AT 25°C

| No.* | $t$ min. | Sample mg. | Sample +$CCl_4$ mg. | $W$ % | $D$ | Yield |
|---|---|---|---|---|---|---|
| 1 | 30 | 45.5 | 5342.3 | 0.851 | — | — |
| 2 | 30 | 46.2 | 5490.0 | 0.841 | — | — |
| 3 | 50 | 41.2 | 4850.6 | 0.850 | 0.122 | 20 |
| 4 | 50 | 45.0 | 5305.0 | 0.848 | 0.105 | 15 |
| 5 | 70 | 35.0 | 4099.5 | 0.854 | 0.183 | 38 |
| 6 | 70 | 44.3 | 5215.3 | 0.851 | 0.144 | 27 |
| 7 | 90 | 44.6 | 5232.6 | 0.852 | 0.257 | 60 |
| 8 | 90 | 44.0 | 5171.0 | 0.850 | 0.227 | 51.5 |

* Odd numbers are from the 3$\beta$-epimer and even numbers from the 3$\alpha$-epimer.

TABLE V. THE OXIDATION OF BOTH EPIMERS FOR 60 min. AT 25°C

| Starting material | Sample mg. | Sample +$CCl_4$ mg. | $W$ % | $D$ | Yield of 3-oxo deriv. % |
|---|---|---|---|---|---|
| 3$\beta$ | 41 | 4.919 | 0.831 | 0.262 | 63.8 |
| 3$\alpha$ | 43.5 | 5.050 | 0.862 | 0.219 | 48.3 |

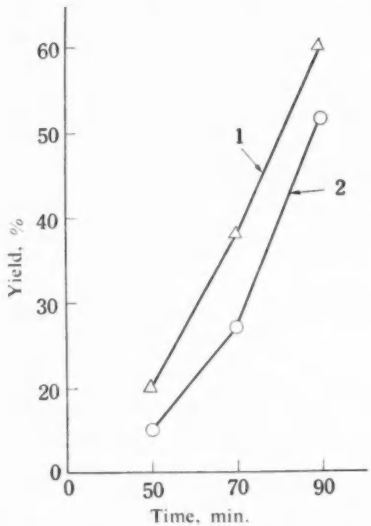



Fig. 3. Relationship between time and yield in each epimer.
(1) 3$\beta$-epimer; (2) 3$\alpha$-epimer

oxidation of epimeric methyl 3-hydroxy-5$\beta$-cholanoates was carried out with 1.3 molar equivalents of NBS in dioxane-water (9:1) solution at 25°C. There is a marked difference in the yield between 3$\beta$- and 3$\alpha$-hydroxyl derivatives (Fig. 3). The values obtained are shown in Tables IV and V. Accordingly, the order of susceptibility to oxidation obtained from the results described above was as follows:

$$6\beta(a) > 3\beta(a) > 3\alpha(e) > 6\alpha(e) \quad (A/B: \text{cis})$$

In order to obtain the further support on the influence of steric factors in this reaction, the oxidation of two 3,6-dihydroxy-5$\alpha$-cholanoic acid (3$\beta$,6$\beta$-dihydroxy-5$\alpha$-cholanoic acid and 3$\beta$,6$\alpha$-dihydroxy-5$\alpha$-cholanoic acid) was examined. The oxidation was carried out as in the previous case. While the oxidation of the former gave a 6-oxo derivative, the oxidation of the latter gave a 3-oxo derivative. From these results in A/B-trans series, the 6$\beta$-hydroxy group was also rapidly oxidized but the 6$\alpha$-hydroxyl group was not affected under such a condition and the ease of oxidation of the 3$\beta$-hydroxyl group was in between. Accordingly, the order of the susceptibility to the oxidation of hydroxyl groups in A/B-trans series was also as follows:

$$6\beta(a) > 3\beta(e) > 6\alpha(e) \quad (A/B: \text{trans})$$

**Discussion on the Reaction Mechanism**

Prior to considering the reaction mechanism of oxidation with NBS from the above result, the outline of reports on the reaction mechanism of chromic acid oxidation should be described. Westheimer and Nicolaides[9] minutely studied the reaction mechanism of chromic acid oxidation and they found that the rate-determining step is not the formation of a chromate ester but the cleavage of the carbon hydrogen bond.

$$(A) \quad R_2CHOH + HCrO_4^- + H^+ \overset{\text{fast}}{\rightleftarrows} R_2CHOCrO_3H + H_2O$$

$$(B) \quad R_2C(H)\text{-}O\text{-}CrO_3H + H_2O \xrightarrow{\text{slow}} R_2C{=}O + [HCrO_3^-] + H_3O^+$$

Barton[10] found that the conformational factor determined nearly always the order of reactivity in oxidation among several hydroxyl groups and established a general rule that an axial alcohol is ordinarily more susceptible than the corresponding equatorial alcohol. There are, however, some cases in which an equatorial alcohol having a less accessible axial carbon hydrogen bond is faster oxidized than an axial alcohol (e.g. compare equatorial 11$\alpha$-hydroxyl with 3-axial hydroxyl group). Schreiber and Eschenmoser[11] measuring the reaction rates of oxidation of a number of hydroxy-5$\alpha$-cholestanes, confirmed again a general rule proposed by Barton and further defined a second factor determining reaction rates. That is, the transformation of the tetrahedral carbon of an alcoholic (or chromate ester) group to a trigonal carbonyl carbon often eliminates some or all of the repulsive interactions leading to instability. The reaction rates are thus dependent upon the extent of decrease in such interactions. A example in A/B-trans series is as follows:

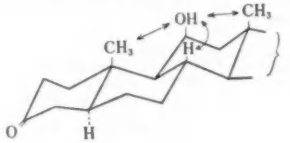



Fig. 4

As seen in Fig. 4, the 11$\beta$-hydroxyl group is under steric strain from the repulsions between the four groups, 11$\beta$-hydroxyl, C-10-methyl, C-13-methyl and 8$\beta$-hydrogen. Relief of this strain provides a driving force sufficient to promote the oxidation.

On the other hand, oxidation with reagents such as *N*-bromosuccinimide or *N*-bromoacetamide has been less clear from both mechanistic and conformational view points[12]. On the basis of the studies described above, the reaction mechanism of oxidation with NBS could be considered. The order of susceptibility to oxidation of the epimeric 3,6-dihydroxycholanoic acids with NBS was as follows:

$$(C) \quad 6\beta(a) > 3\beta(a) > 3\alpha(e) > 6\alpha(e) \quad (A/B: \text{cis})$$

$$(D) \quad 6\beta(a) > 3\beta(e) > 6\alpha(e) \quad (A/B: \text{trans})$$

On the other hand, the order in chromic acid oxidation of hydroxy-5$\alpha$-cholestanes by Schreiber at the corresponding position was as follows:

$$(E) \quad 6\beta(a) > 3\alpha(a) > 6\alpha(e) > 3\beta(e)$$
$$[36]^* \quad [3.0]^* \quad [2.0]^* \quad [1.0]^* \quad (A/B: \text{trans})$$

* Relative rates to 3$\beta$-hydroxy-5$\alpha$-cholestane.

From the results on the oxidation of $\alpha$-hyodeoxycholic acid with chromic acid, there are also the following positions.

9) F. H. Westheimer and N. Nicolaides, ibid., **71**, 25 (1949).
10) D. H. R. Barton, *Experientia*, **6**, 316 (1950); *J. Chem. Soc.*, **1953**, 1027.
11) J. Schreiber and A. Eschenmoser, *Helv. Chim. Acta*, **38**, 1929 (1955).
12) H. J. E. Loenthal, *Tetrahedron*, **6**, 269 (1959).

(F) $6\alpha(e) > 3\alpha(e)$ (A/B: cis)

Compared with the above cited four expressions C, D, E and F, it is analogous in conformational view in accord with the Barton rule. In other words, an axial alcohol is more susceptible to oxidation than the corresponding equatorial epimer ($6\beta > 6\alpha$, $3\beta > 3\alpha$: A/B cis). Accordingly, in the case of the axial hydroxyl group, it is clear that the oxidation with NBS proceeds likewise to chromic acid oxidation, because both intermediates similarly have a more accessible C–H bond (equatorial) and a repulsive intermediate ester (axial). The concept described above will be also supported by the following examples.

cholestane-3$\beta$, 5$\alpha$, 6$\beta$-triol—
6-oxo derivative[13]

3$\beta$, 6$\beta$-dihydroxy-5$\alpha$-cholanoic acid—
6-oxo derivative*2

5$\alpha$-cholestane-3$\beta$, 7$\alpha$-diol—
7-oxo derivative[14]

11$\beta$-hydroxytigogenine—11-oxo derivative[15]

11$\beta$-hydroxyprogesterone—
11-oxo derivative[16]

(11$\alpha$-hydroxyprogesterone was not affected under same condition).

On the other hand, in the series of the generally less reactive equatorial hydroxyl group, e.g. in the case of $\alpha$-hyodeoxycholic acid, the order with NBS was the reverse of that with chromic acid as seen in expressions C and F. This difference is supposed to depend on a driving force in the intermediate, because it is clear that the conformation of C–H bond (e.g. the 6$\beta$-H in Figs. 5 and 6) is equivalent in each case. In the chromic acid oxidation, the intermediate ester has a strong driving force which is derived from both a large space-claim ("Raumbeanspruchung") and an inductive factor (Fig. 5). On the other hand, in the oxidation with NBS, it is assumed that the intermediate ester has a little driving force which resulted from a smaller space-claim and from almost no inductive factor. (Fig. 6). The further explanation was as follows: in the chromic acid oxidation, since the 6$\beta$-hydrogen suffers the driving force sufficient to promote the reaction as mentioned above, it can be more easily eliminated than the 3$\beta$-hydrogen, whereas in the case of NBS, the driving force of the intermediate hypohalite is very insufficient. For this reason, an attack of the base on a hydrogen atom attached to the hydroxyl carbon is indispensable for the promotion of the reaction as well as the elimination of this hydrogen. Consequently, it may be deduced that the most important factor in the oxidation of the less reactive equatorial alcohol with NBS depends upon the extent of easiness of the proximity of base to the C–H bond of the alcoholic carbon being oxidized. Therefore, in the oxidation of $\alpha$-hyodeoxycholic acid with NBS, the 3$\alpha$-hydroxyl group is more easily oxidized than the 6$\alpha$-hydroxyl group owing to the vulnerability of the 3$\beta$-hydrogen. This concept may be further supported by the fact that the less accessible C–H bonds such as in the 6$\alpha$- or 11$\alpha$-alcohol are not affected.

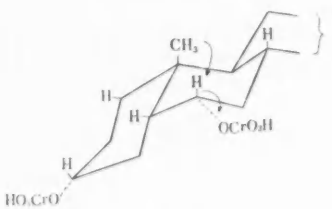



Fig. 5

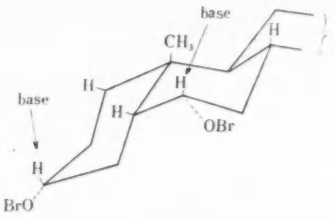



Fig. 6

Examples which show the concept described above are as follows:

3$\beta$, 6$\alpha$-dihydroxy-5$\alpha$-cholanoic acid—
3-oxo derivative*2

5$\beta$-androstane-3$\alpha$, 11$\alpha$, 17$\beta$-triol—
3, 17-dioxo derivative[17]

11$\alpha$-hydroxypregnane-3, 20-dione is recovered unchanged after treatment with *t*-butylhypochlorite.

3$\beta$, 11$\alpha$-dihydroxy-5$\alpha$-pregnan-20-one—
3, 20-dioxo derivative[18]

That desoxycholic acid was not affected with

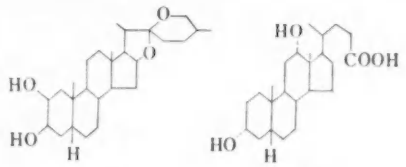
13) L. F. Fieser and S. Rajagopalan, *J. Am. Chem. Soc.*, **71**, 3938 (1949).
*2 See experimental part.
14) L. F. Fieser and S. Rajagopalan, ibid., **74**, 3309 (1952).
15) S. G. Brooks, J. S. Hunt, A. G. Long and B. Mooney, *J. Chem. Soc.*, **1957**, 1175.
16) A. R. Hanze, G. S. Fonken, A. V. McIntosch, A. M. Searcy and R. H. Levin, *J. Am. Chem. Soc.*, **76**, 3179 (1954).
17) H. L. Herzog, M. Jevnik, and E. B Hershberg, ibid., **75**, 269 (1953).
18) O. Mancera, J. Romo, F. Sondheimer, G. Rosenkranz and C. Djerassi, *J. Org. Chem.*, **17**, 1066 (1952).

NBS in aqueous acetone or in aqueous sodium hydrogen carbonate[19] but with NBA in aqueous *t*-butanol[20], certainly appears to be governed principally by steric effects coupled with size of the reagent and solvating power of the solvent. Thereupon, all hydroxyl groups in which $\alpha$-hydrogen permits the approach of the base, should be oxidized and this theory was also supported by the following examples.

Ethyl 3$\beta$, 5$\beta$, 19-trihydroxyetianate—3-oxo derivative[21]

Methyl 3$\alpha$-hydroxy-9$\alpha$, 11$\alpha$-epoxy-5$\beta$-cholanoate—3-oxo derivative[22]

The hydroxyl group at $C_3$ in samogenine[23] (I) and in desoxycholic acid[19] (II), however, was not affected with NBS The reason is not clear in details but it perhaps depends upon the intermediate permitting no release of $\alpha$-hydrogen on account of vicinal effect or another interactions.




(I) (II)

## Experimental[24]

**Oxidation of Epimeric 3, 6-Dihydroxy-5$\beta$-cholanoic Acids with NBS**—General procedure of oxidation was performed by almost the same means as the method previous described[2].

**1) The Case of $\alpha$-Hydroxycholic Acid.**—*1.1) With 1 Molar Equivalent of NBS in Dioxane-Water.*—A mixture consisting of $\alpha$-hyodeoxycholic acid (761 mg.), dioxane-water (9 : 1) (15 ml.) and NBS. (380 mg.; 1.1 mol. equiv.) was allowed to stand for 1.5 hr. at room temperature (18°C). The mixture was changed from colorless to yellow and to orange successively in coloration. To the solution, 10% of aqueous sodium bisulfite was added. The ether extract was washed well with water and evaporated to dryness to afford oil (920 mg.) which was followed by esterification with methanol (4 ml.) and 10% of methanolic hydrochloric acid (0.5 ml.) overnight at room temperature. The ether extract, after isolation in the usual way, gave a yellow oil (777 mg.) which was chromatographed on alumina to afford methyl 3-oxo-6$\alpha$-hydroxy-5$\beta$-cholanoate 3-acetal, 237 mg. (27.2%), m. p. 153~154°C. Identity was established by a mixed melting point and the infrared spectrum with the authentic sample. Infrared spectrum: $\nu_{max}$ 3564 (OH); 1724 cm$^{-1}$ (C=O).

Found: C, 72.10; H, 10.30. Calcd. for $C_{27}H_{46}O_5$: C, 71.96; H, 10.29%.

*1.2) With 2 Molar Equivalents of NBS in Dioxane-Water.*—A mixture consisting of $\alpha$-hyodeoxycholic acid (605 mg.), dioxane-water (9 : 1) (10 ml.) and NBS (600 mg.; 2.2 mol. equiv.) was treated as in the previous case. The mixture gave methyl 3-oxo-6$\alpha$-hydroxy-5$\beta$-cholanoate 3-acetal, m. p. 152~153°C, 209 mg. (30.1%). This compound was identified by a mixed melting point and the infrared spectrum with the authentic sample.

*1.3) With 1 Molar Equivalent of NBS in Acetone-Water.*—A mixture consisting of $\alpha$-hyodeoxycholic acid (579 mg.), acetone-water (7 : 3) (13 ml.) and NBS (290 mg.; 1.1 mol. equiv.) was treated as in the previous case after being allowed to stand overnight at room temperature to furnish crystals, 224 mg., m. p. 146~151°C. The residue from the filtrate was chromatographed on alumina in the usual manner to afford the acetal with m. p. 149~151°C (53 mg.). Total yield were 41.7%. This sample was also identical in a mixed melting point and the infrared spectrum.

*1.4) With 2 Molar Equivalents of NBS in Acetone-Water.*—The mixture consisting of $\alpha$-hyodeoxycholic acid (929 mg.), pyridine (500 mg.), acetone-water (7 : 3) (20 ml.) and NBS (926 mg.; 2.2 mol. equiv.) was treated in a way similar to that of the case in the preceding section after being kept for four days at room temperature (20°C) to give the acetal with m. p. 150~152°C (660 mg.; 61.8%). Identity was established by a mixed melting point and the infrared spectrum. Found: C, 72.16; H, 10.26%.

**2) The Case of $\beta$-Hyodeoxycholic Acid.**—*2.1) With 1 Molar Equivalent of NBS in Dioxane-Water.*—After treatment as in the case of section 1.1 the above acetal with m. p. 152~153°C was obtained in 21.3% yield. This compound was identical with the authentic methyl 3-oxo-6$\alpha$-hydroxy-5$\beta$-cholanoate 3-acetal in a mixed melting point and the infrared spectrum.

*2.2) With 2 Molar Equivalents of NBS in Dioxane-Water.*—Treatment as in the case of section 1.2 afforded the acetal with m. p. 150~152°C in 45.7% yield. Identification was carried out by a mixed melting point and the infrared spectrum.

*2.3) With 1 Molar Equivalent of NBS in Acetone-Water.*—Treatment similar to that in the case of section 1.3 gave the acetal with m. p. 150~152°C in 31% yield. This compound was also identified

19) L. F. Fieser and S. Rajagopalan, *J. Am. Chem. Soc.*, **71**, 3535 (1949).
20) H. Reich and T. Reichstein, *Helv. Chim. Acta*, **26**, 562 (1943).
21) P. Herzig and M. Ehrenstein, *J. Org. Chem.*, **17**, 713 (1952).
22) L. F. Fieser and S. Rajagopalan, *J. Am. Chem. Soc.*, **73**, 118, 5252 (1951).
23) H. Ōsaka, private communication.
24) All melting points are uncorrected. Infrared spectra were recorded in Nujol Mulls with a "Koken DS 301" double beam infrared spectrophotometer, unless otherwise noted, and the ultraviolet spectra were taken in 95% ethanol solution using a "Hitachi EPS 2" spectrophotometer. Optical rotations were determined in a 1-dm. tube for chloroform solutions, unless otherwise specified. Alumina used for chromatography in this experiment was Merk's reagent grade standardized according to Brockmann and the chromatography was usually performed according to the method described by T. Reichstein. (T. Reichstein and W. Schoppee, *Diss. Faraday Soc.*, **1949**, 305) Extracts were dried over anhydrous sodium sulfate before evaporation unless stated otherwise.

by a mixed melting point and the infrared spectrum.

*2.4) With 2 Molar Equivalents of NBS in Acetone-Water.*—Isolation similar to that in the case of section 1.4 furnished the acetal with m. p. 148~150°C in 62.5% yield. Identity was established by a mixed melting point and the infrared spectrum.

**3) The Case of 3β,6β-Dihydroxy-5β-cholanoic Acid.**—In this experiment, methyl 3β, 6β-dihydroxy-5β-cholanoate was used on account of insolubility of its acid in acetone-water (7 : 3).

*3.1) With 1 Molar Equivalent of NBS in Dioxane-Water.*—A mixture consisting of methyl 3β, 6β-dihydroxy-5β-cholanoate (350 mg.), dioxane-water (9 : 1) (10 ml.) and NBS (169 mg.; 1.1 mol. equiv.) was allowed to stand for 1.5 hr. at room temperature (22°C). To the solution, 10% of aqueous sodium bisulfite was added to decolorize it. The extract with ether was washed well with water and evaporated to dryness to yield orange oil (494 mg.) which was acetylated with pyridine (4 ml.) and acetic anhydride (4 ml.) under reflux for 2 hr. After cooling, the mixture was carefully diluted with water to afford crystals which were collected, washed throughly with water and recrystallized from methanol to methyl 3β-acetoxy-6-oxo-5α-cholanoate, 235 mg., scales, m. p. 156~158°C. Ether extraction from the above aqueous and methanolic filtrate afforded a yellow oil (156 mg.) which was followed by chromatography on alumina. The eluate with petroleum ether-benzene (2 : 8 and 1 : 1) and benzene gave the above 6-oxo derivative with m. p. 157.5~158°C (61 mg.). Total yield was 77%. This compound was identified by a mixed melting point and the infrared spectrum with the authentic methyl 3β-acetoxy-6-oxo-5α-cholanoate. $[\alpha]_D^{24} = -14 \pm 2°$ (*c* 1.038). Infrared spectrum: $\nu_{max}$ 1730, 1710 (C=O); 1252, 1239, 1169, 1039 $cm^{-1}$ (C-O).

Found: C, 72.65; H, 9.48. Calcd. for $C_{27}H_{42}O_5$: C, 72.61; H, 9.48%.

*3.2) With 2 Molar Equivalents of NBS in Dioxane-Water.*—A mixture consisting of methyl 3β, 6β-dihydroxy-5β-cholanoate (347 mg.) dioxane-water (9 : 1) (10 ml.) and NBS (320 mg.; 2.1 mol. equiv.) was treated as in the previous subsection to give an orange oil (413 mg.) which was followed by chromatography on alumina. The eluate with benzene-petroleum ether (1 : 1), benzene and benzene-chloroform (9 : 1) furnished methyl 3β-acetoxy-6-oxo-5α-cholanoate, 216 mg. (56.6%), scales, m. p. 158~159°C. This was identical with the above specimen in a mixed melting point and the infrared spectrum. The benzene-chloroform (8 : 2 and 1 : 1) elution afforded methyl 3,6-dioxo-5α-cholanoate, 49 mg. (14.3%), m. p. 146~148°C. Zimmermann test gave cherry-red coloration. Infrared spectrum: $\nu_{max}$ 1745, 1711 $cm^{-1}$ (C=O).

Found: C, 74.19; H, 9.58. Calcd. for $C_{25}H_{38}O_4$: C, 74.59; H, 9.52%.

*3.3) With 1 Molar Equivalent of NBS in Acetone-Water.*—Isolation as in the section 3.1 after being kept overnight at room temperature (18°C) gave methyl 3β-acetoxy-6-oxo-5α-cholanoate, m. p. 157~158°C in 77.5% yield. Zimmermann test was negative. This compound was also identical with the above specimen by a mixed melting point and the infrared spectrum.

*3.4) With 2 Molar Equivalents of NBS in Acetone-Water.*—Treatment as in the previous case furnished methyl 3β-acetoxy-6-oxo-5α-cholanoate, m. p. 157~158°C in 55% yield from the elution with benzene-petroleum ether (1 : 1) and benzene, and methyl 3,6-dioxo-5α-cholanoate, m. p. 148°C in 19.3% yield from the benzene-chloroform (9 : 1) eluate. These samples were also identified by a mixed melting point and the infrared spectrum.

**4) The Case of 3α,6β-Dihydroxy-5β-cholanoic Acid.**—*4.1) With 1 Molar Equivalent of NBS in Dioxane-Water.*—To a solution of 3α,6β-dihydroxy-5β-cholanoic acid (377 mg.) in dioxane-water (9 : 1) (10 ml.), NBS (188 mg.; 1.1 mol. equiv.) was added and kept for 1.5 hr. at room temperature (20±2°C). Isolation, esterification with ethereal diazomethane and acetylation in the usual way gave methyl 3α-acetoxy-6-oxo-5β-cholanoate as prisms, m. p. 150~153°C, 260 mg. $[\alpha]_D^{17} = -21 \pm 2°$ (*c* 1.052, dioxane). Infrared spectrum: $\nu_{max}$ 1703 (C=O); 1241, 1230, 1164, 1036, 1026 $cm^{-1}$ (C-O).

Found: C, 72.62; H, 9.59. Calcd. for $C_{27}H_{42}O_5$: C, 72.61; H, 9.48%.

By chromatography on alumina, the filtrate from the above crystals gave further 6-oxo derivative, 40 mg., m. p. 155~165°C (from methanol), a mixture of 5α- and 5β-series.

Found: C, 72.71; H, 9.53%. Total yield was 70%.

*4.2) With 2 Molar Equivalents of NBS in Dioxane-Water.*—Isolation in the usual way gave a mixture of 6-oxo derivative in 5α- and 5β-series with m. p. 143~147°C in 60% yield from the eluate with benzene-petroleum ether (1 : 1), benzene and benzene-chloroform (9 : 1). Infrared spectrum: $\nu_{max}$ 1741, 1712 (C=O); 1249, 1175, 1025 $cm^{-1}$ (C-O).

Found: C, 72.75; H, 9.43. Calcd. for $C_{27}H_{42}O_5$: C, 72.61; H, 9.48%.

The benzene-chloroform (8 : 2 and 1 : 1) eluate gave methyl 3,6-dioxo-5α-cholanoate, m. p. 146~148°C, in 7.5% yield. Infrared spectrum: $\nu_{max}$ 1740, 1710 (C=O); 1171 $cm^{-1}$ (C-O).

Found: C, 74.19; H, 9.64. Calcd. for $C_{25}H_{38}O_4$: C, 74.59; H, 9.52%.

*4.3) With 1 Molar Equivalent of NBS in Acetone-Water.*—The methyl ester was used in this case because the acid was not dissolved in acetone-water (7 : 3). Treatment as in section 3.3 gave 6-oxo derivative, m. p. 150~155°C, in 70% yield. The identification was carried out by a mixed melting point and the infrared spectrum.

Found: C, 72.55; H, 9.64%.

*4.4) With 2 Molar Equivalents of NBS in Acetone-Water.*—Reaction and isolation as in section 3.4 afforded 6-oxo derivatives in 5α- and 5β-series with m. p. 155~160°C and m. p. 169~170°C, respectively in 59.4% yield from the eluate with benzene and benzene-chloroform (9 : 1). Zimmermann test was negative. Identity was established by a mixed melting point and the infrared spectrum.

Found: C, 72.92; H, 9.57%.

Benzene-chloroform (9 : 1) elution gave methyl 3,6-dioxo-5β-cholanoate, m. p. 128~129°C, in 16% yield. Infrared spectrum: $\nu_{max}$ 1739, 1712 (C=O), 1171 $cm^{-1}$ (C-O).

Found: C, 74.07; H, 9.44%.

**Oxidation of 3β, 6α-Dihydroxy-5α-cholanoic Acid**[*3]. — To a solution of 3β,6α-dihydroxy-5α-cholanoic acid (140 mg.) and pyridine (37.3 mg.) in acetone (1.96 ml.) and water (0.84 ml.) was added NBS (82.5 mg.; 1.3 mol. equiv.). The resulting mixture was refluxed for 4.5 hr., and then the solvent was removed under reduced pressure to the point of distinct turbidity. After a large volume of water was added, the precipitate was collected and dried. This crude keto acid (46 mg.) was recrystallized from acetone to afford 3-oxo-6α-hydroxy-5α-cholanoic acid, fine needles, m. p. 195~197°C (20 mg.). Zimmermann test was positive. $[\alpha]_D^{32}$ = +4±2° (*c* 1.059, pyridine).

Found: C, 73.21; H, 9.85. Calcd. for $C_{24}H_{38}O_4$: C, 73.80; H, 9.81%.

The above crude acid was esterified with ethereal diazomethane to yield its methyl ester, melting at 90~97°C undefinitely. Zimmermann test was positive. $[\alpha]_D^{27}$ = +55±2° (*c* 1.038). Infrared spectrum: $\nu_{max}^{CHCl_3}$ 3524 (OH); 1731, 1711 $cm^{-1}$ (C=O).

Found: C, 72.86; H, 10.04. Calcd. for $C_{25}H_{40}O_4 \cdot 1/2H_2O$: C, 72.61; H, 9.91%.

Acetylation of this methyl ester gave methyl 3-oxo-6α-acetoxy-5α-cholanoate, plates, m. p. 115~116°C (from ether-petroleum ether). Zimmermann test was positive. $[\alpha]_D^{33}$ = +48±4° (*c* 0.608)*[4]. Infrared spectrum: $\nu_{max}^{CHCl_3}$ 1729, 1712 (C=O); 1249, 1175, 1024 $cm^{-1}$ (C-O).

Found: C, 72.92; H, 9.81. Calcd. for $C_{27}H_{42}O_5$: C, 72.61; H, 9.48%.

**Oxidation of 3β, 6β-Dihydroxy-5α-cholanoic Acid**[*5]. — To a solution of 3β,6β-dihydroxy-5α-cholanoic acid (73 mg.) in acetone (6 ml.), water (1 ml.) and methanol (1.5 ml.), was added NBS (75 mg.; 2.3 mol. equiv.). After the resulting mixture was kept for 3 hr. at room temperature, aqueous sodium bisulfite was added, and the extract with ether was washed with water and evaporated to furnish needles with m. p. 235~237°C. This crude acid was recrystallized from acetone to methyl 3β-hydroxy-6-oxo-5α-cholanoic acid, m. p. 244~245°C, 23 mg. Zimmermann test was negative. Ultraviolet spectrum: $\lambda_{max}^{EtOH}$ 287 mμ (ε=45). Infrared spectrum: $\nu_{max}$ 1727, 1689 $cm^{-1}$ (C=O).

Found: C, 73.61; H, 9.68. Calcd. for $C_{24}H_{38}O_4$: C, 73.80; H, 9.81%.

Its methyl ester was obtained as scales from methanol, melting at 93~95°C. Acetylation of this methyl ester furnished methyl 3β-acetoxy-6-oxo-5α-cholanoate, m. p. 155~157°C, scales. A mixed melting point with methyl 3α-acetoxy-6-oxo-5β-cholanoate with m. p. 156~157°C was melted at 130~135°C. $[\alpha]_D^{32}$ = −9±2° (*c* 0.91, methanol).

Found: C, 72.62; H, 9.45. Calcd. for $C_{27}H_{42}O_5$: C, 72.61; H, 9.48%.

*3 Synthesis of this compound was described in preceding part XX.

*4 Optical rotation of methyl 3-oxo-6α-acetoxy-5β-cholanoate was as follows: $[\alpha]_D^{31}$ = −29±2° (*c* 1.057).

*5 As optical rotation of this compound had not been reported, it was measured by the author and its value was found to be as follows: $[\alpha]_D^{33}$ = −0.1±2° (*c* 1.057, pyridine).

**Spectroscopic Determination of the Order of Reactivity in the Oxidation of Methyl 3β- and 3α-Hydroxy-5β-cholanoate with NBS.** — *Measurement.*—For the measurement of the optical densities, a "Koken DS 301" (double beam) was used. Infrared spectra were measured by used of a 0.25 mm. cell and at the concentration of about 37% transmission of carbonyl stretching absorption band of the ester group which was controlled by dilution. The speed in the measurements was adjusted to 50 $cm^{-1}$ per 36 sec. at about 1700 $cm^{-1}$ for the purpose of a quantitative analysis. The optical densities of carbonyl band at 1720 $cm^{-1}$ in carbon tetrachloride solution was calculated by the base line method (Fig. 1). $T_0$ and $T$ were a mean value of three measurements.

*Procedure.* — A mixture consisting of 3-hydroxy compounds (210 mg.), NBS (126 mg.; 1.3 mol. equiv.) and dioxane-water (9:1) (22 ml.) in a 50 ml. reaction flask with stopper was allowed to stand at 25°C with use of thermostat. Each 5 ml. of the reaction mixture was pipetted at various times and the reaction in each aliquot was stopped with aqueous sodium bisulfite, extracted with ether and successively washed with water, soda and water (ten times). The ethereal layers were evaporated and finally dried in vacuo for 12 hr. at 60°C. The obtained residue (about 45 mg.) was dissolved in so much carbon tetrachloride as to make an adequate concentration giving optical density of the carbonyl band in the ester group at about 37% transmission. The yield of the oxidation product was estimated from the calibration curve prepared above (Fig. 2). These values are shown in Tables IV and V (Fig. 3).

## Summary

(1) The order of susceptibility of the hydroxyl groups in epimeric 3,6-dihydroxy-cholanoic acids to the oxidation with NBS was determined and the results were as follows:

6β(a) > 3β(a) > 3α(e) > 6α(e) (A/B: cis)

6β(a) > 3β(e) > 6α(e) (A/B: trans)

(2) Reaction mechanism of the oxidation with NBS was discussed.

The author is particularly indebted to Dr. K. Takeda, Director of this Laboratory, for his discussions and encouragement during this work. The author gratefully acknowledges many helpful discussions with Dr. W. Nagata. Thanks are also due to Mr. Y. Matsui for infrared spectral measurements, to Messers T. Ieki, K. Miyahara, K. Daikatsu, T. Takaoka and Miss. U. Kasugai for elementary analyses and to Mr. T. Iwata for measurements of optical rotation.

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# *Mineral Content of Mixed Fertilizer*

By Jumpei ANDO and Seiichi MATSUNO

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Recently in Japan nearly 1200000 tons of mixed fertilizer has been produced yearly by the following process:—calcium superphosphate, ammonium sulfate and potassium chloride are mixed, ammoniated so as to neutralize the free phosphoric acid in superphosfate, granulated between 3 and 20 meshes with sprayed water, dried in a rotary drier so as to have 2~3% free water, cooled to 40~60°C by rotary cooler, kept in storage pile for days or weeks and then packed. Ikeno[1] reported that ammonium syngenite and monoammonium phosphate were formed in 8-8-7 mixed fertilizer. No other report is found concerning the fertilizer.

In the present work the mineral content of the products having various $N : P_2O_5 : K_2O$ ratios and reactions during the production process were investigated so as to clarify the cause of caking of products which often takes place in the storage pile, the action of water in the products which must be known for calculation of material balance, and other problems concerning the fertilizer have been studied.

## Experimental and Results

**Mineral Content of Products.**—It was clarified by X-ray diffraction that commercial mixed fertilizers (Table I) were mainly composed of potassium ammonium syngenite (crystalline solution of potassium syngenite $K_2SO_4 \cdot CaSO_4 \cdot H_2O$ and ammonium syngenite $[(NH_4)_2SO_4 \cdot CaSO_4 \cdot H_2O]$, monoammoniumpotassium phosphate (crystalline solution of monoammonium phosphate $NH_4H_2PO_4$ and monopotassium phosphate $KH_2PO_4$), ammonium chloride and calcium sulfate anhydride. The minerals used as raw materials such as monocalcium phosphate monohydrate, ammonium sulfate and potassium chloride were not at all or were only slightly detected in the products. The amount of these minerals in the products was determined by X-ray diffractometer using spinel $MgO \cdot Al_2O_3$ as inner standard.

**Synthesis of Standard Samples.**—a) *Inner Standard.*—By preliminary tests it was found that spinel $MgO \cdot Al_2O_3$ was suitable as inner standard. A mixture of equal mole of refined magnesia and alumina was heated for 30 min. at 1600~1670°C. Spinel was formed almost completely. The product contained very few other minerals.

b) *Calcium Sulfate Anhydride.*—Calcium carbonate was treated with concentrated sulfuric acid.

c) *Syngenite.*—Ammonium sulfate or potassium sulfate or various mixtures of both of these was mixed with a theoretical amount of calcium sulfate anhydride and excess of water, heated at 45°C on a water bath and dried. Addition of water and drying were repeated until the single salts disappeared and syngenite or a homogeneous crystalline solution of syngenite was formed.

d) *Monoammoniumpotassium Phosphate.*—Monoammonium phosphate and monopotassium phosphate were mixed at various ratios, the mixture being wet with water, heated at 45°C on water bath

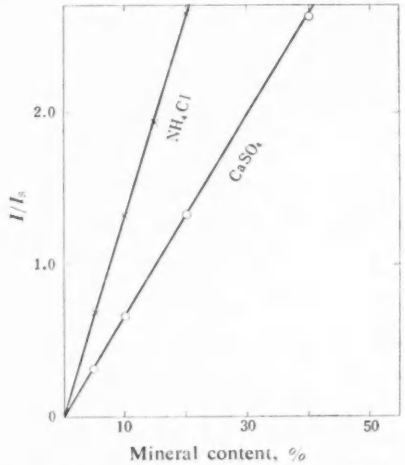


Fig. 1. Calibration curves of ammonium chloride and calcium sulfate anhydride.

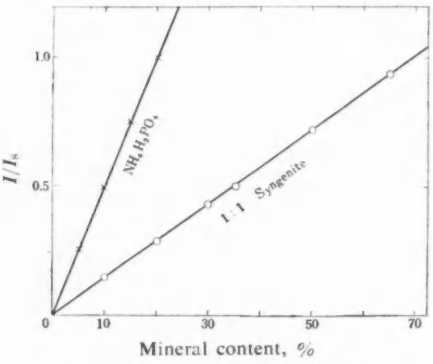


Fig. 2. Calibration curves of monoammonium phosphate and 1 : 1 syngenite.

1) R. Ikeno and Y. Shimomura, *J. Chem. Soc. Japan, Ind. Chem. Sec.* (*Kogyo Kagaku Zasshi*), **63**, 78 (1960).

and dried. A homogeneous crystalline solution was formed easily.

**Method of Determination.**—The Amount of each salt was determined measuring the diffraction peaks of the following angle ($2\theta$ by Cu ray): spinel 36.8°, crystalline solution of syngenite around 9°, monoammoniumpotassium phosphate around 16.6°, ammonium chloride 32.6°, calcium sulfate anhydride 25.4°, ammonium sulfate 20.4° and potassium chloride 28.3°. One handred parts of a mixture of 1 : 1 syngenite (crystalline solution of ammonium and potassium syngenite 1 : 1 by weight), monoammonium phosphate, ammonium chloride and calcium sulfate anhydride were mixed with 25 parts

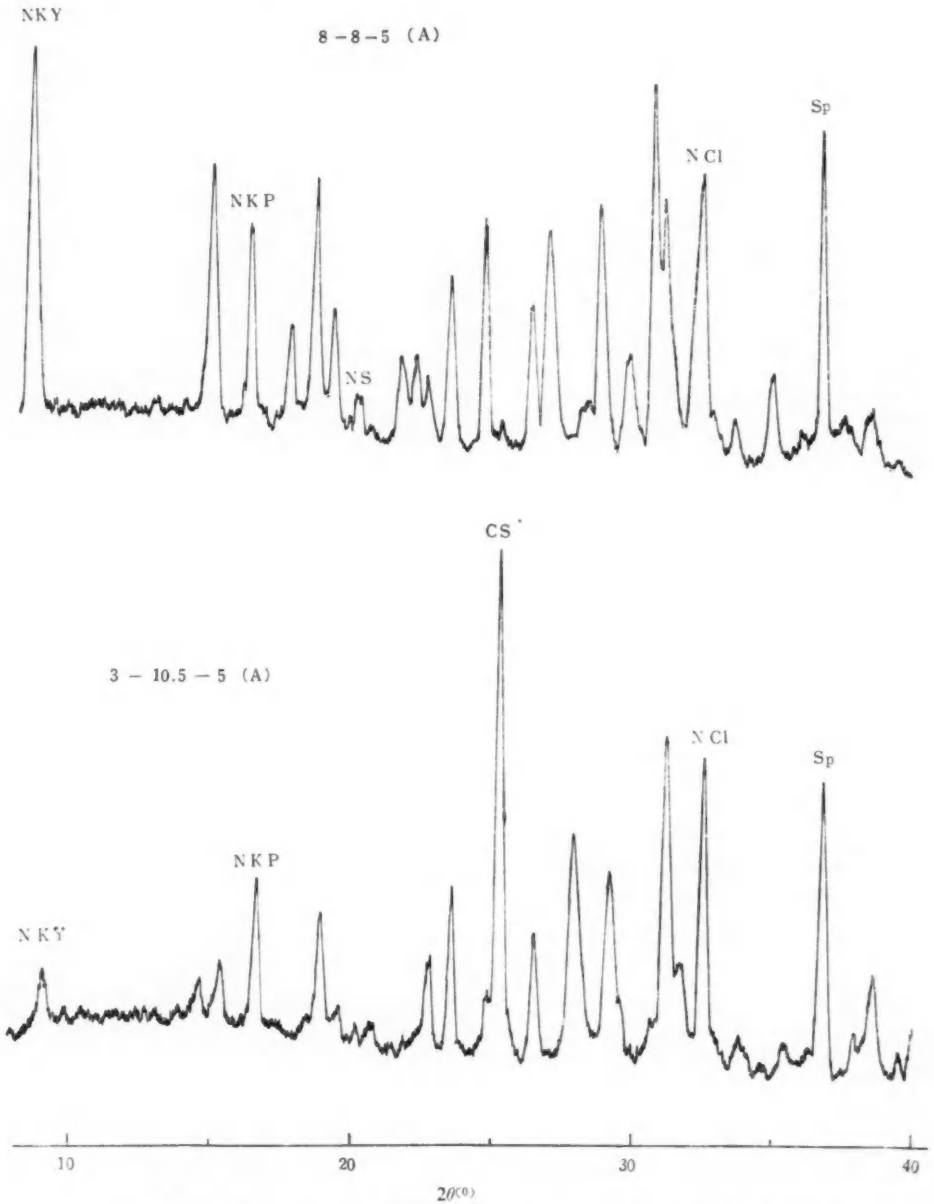


Fig. 3. X-ray diffraction patterns of mixtures of commercial fertilizers, 100 parts, and spinel, 25 parts (Cu ray, Ni filter).

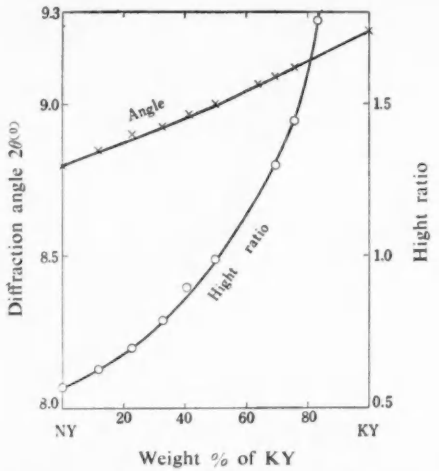


Fig. 4. Relation between weight ratio of ammonium syngenite (NY) component and potassium syngenite (KY) component in their crystalline solution and diffraction angle of center of the peak and also the ratio of height of the peak of 1 : 1 syngenite and that of other syngenite.

of spinel and were recorded by X-ray diffractometer. Calibration curves thus obtained are illustrated in Figs. 1 and 2.

One handred parts of mixed fertilizer and 25 parts of spinel were mixed and recorded by X-ray diffractometer (Fig. 3). The content of ammonium chloride and of calcium sulfate anhydride were determined by Fig. 1.

Figure 4 or 6 was plotted by measurement of various crystalline solution of syngenite or phosphate. The $NH_4/K$ ratio and amount of syngenite or phosphate in commercial fertilizer were determined using the relations of Figs. 2 and 4 or 6.

Results of determination of commercial fertilizer are shown in Table I. These samples contained 1~3% free water measured by weight loss on heating for 3 hr. at 100°C (Table II). A small part of salt was dissolved in the water and was not determined by X-ray. A sample 3-10-10 (C) contained a considerable amount of potassium chloride which was not detected in other samples. The samples contained less than 3% ammonium sulfate. No monocalcium phosphate monohydrate was detected in any sample. Considering these facts together with the results of Table II it is known that the quantitative analysis by X-ray was performed fairly accurately.

**Reactions during Production Process.**—Mixed fertilizer 8-8-6 was prepared in the laboratory under conditions similar to that of a large scale plant.

TABLE I. MINERAL CONTENT (%) OF COMMERCIAL MIXED FERTILIZER PRODUCED IN THREE PLANTS (A, B and C)

| Sample | $CaSO_4$ | $NH_4Cl$ | NKP | | | NKY | | | Total |
|---|---|---|---|---|---|---|---|---|---|
| | | | Sum | NP | KP | Sum | NY | KY | |
| 8-8-5 (A) | 1.7 | 6.5 | 12.5 | 11.9 | 0.6 | 58.8 | 41.2 | 17.6 | 81.0 |
| 6-9.5-5 (A) | 12.3 | 6.7 | 14.8 | 14.1 | 0.7 | 44.8 | 28.0 | 16.8 | 78.6 |
| 3-10.5-5 (A) | 27.5 | 8.5 | 15.6 | 11.2 | 4.4 | 24.6 | 5.7 | 18.9 | 76.2 |
| 8-8-5 (B) | 6.7 | 6.5 | 14.1 | 14.1 | 0 | 51.8 | 36.2 | 15.6 | 80.7 |
| 8-8-6 (C) | 3.4 | 7.2 | 14.7 | 14.3 | 0.4 | 66.4 | 41.5 | 24.9 | 91.7 |
| 8-7-8 (C) | 3.3 | 10.5 | 12.2 | 12.0 | 0.2 | 65.8 | 33.2 | 32.6 | 91.8 |
| 6-9-6 (C) | 20.1 | 7.5 | 14.8 | 13.8 | 1.0 | 47.7 | 25.3 | 22.4 | 90.1 |
| 8-7-8 (C) | 3.4 | 11.5 | 13.1 | 12.9 | 0.2 | 57.3 | 30.4 | 26.9 | 85.3 |
| 3-10-10 (C) | 31.6 | 5.7 | 21.6 | 15.0 | 6.6 | 25.3 | 4.8 | 20.5 | 84.2 |

NP=monoammonium phosphate, KP=monopotassium phosphate,
NKP=crystalline solution of NP and KP, NY=ammonium syngenite, KY=potassium syngenite,
NKY=crystalline solution of NY and KY

TABLE II. COMPARISON OF N, $P_2O_5$ AND $K_2O$ CONTENT DETERMINED BY CHEMICAL ANALYSIS (G) AND BY X-RAY ANALYSIS (X) OF TABLE I

| Sample | N | | $P_2O_5$ | | $K_2O$ | | Free water |
|---|---|---|---|---|---|---|---|
| | X | G | X | G | X | G | |
| 8-8-5 (A) | 6.88 | 8.76 | 7.65 | 8.79 | 5.55 | 5.56 | 3.0 |
| 6-9.5-5 (A) | 5.92 | 6.96 | 9.07 | 10.34 | 5.35 | 5.53 | 3.1 |
| 3-10.5-5 (A) | 4.07 | 4.05 | 9.21 | 10.61 | 7.26 | 7.68 | 5.5 |
| 8-8-5 (B) | 6.46 | 8.50 | 8.70 | 9.10 | 4.74 | 5.31 | 1.4 |
| 8-8-6 (C) | 7.11 | 8.33 | 9.04 | 9.10 | 7.70 | 6.25 | 0.8 |
| 8-7-8 (C) | 7.00 | 8.01 | 7.54 | 7.53 | 9.98 | 10.01 | 1.9 |
| 6-9-6 (C) | 5.78 | 6.02 | 9.03 | 9.10 | 7.16 | 7.20 | 2.2 |
| 8-7-8 (C) | 7.13 | 8.70 | 8.10 | 8.12 | 8.25 | 8.60 | 0.9 |
| 3-10-10 (C) | 3.72 | 3.80 | 12.70 | 11.46 | 6.47 | 10.70 | 2.5 |

The mineral content of samples during the course of preparation was determined by X-ray. Samples of each process in a large scale plant were investigated, too.

Superphosphate (−20 mesh, $P_2O_5$ 17.56%, free water 12.02%) 356 g., potassium chloride (red colored, −42 mesh) 73.5 g. and ammonium sulfate (−42 mesh) 266 g. were mixed and put in a porcelain rotary drum (26×26 cm.). After 74 cc. of 4.75% aqueous ammonia and 15 cc. of water were sprayed the mixture was granulated between 4 and 10 mesh and dried in an air oven at 130°C for 15, 30, 45 and 60 min. Fifty grams of the sample dried for 60 min. (containing 2.91% free water) was put in a 50 cc. stoppered bottle and kept at 50°C for 5 days and then at room temperature for 10 days. The mineral content of samples just after mixing, granulation, drying and keeping for each time were determined by X-ray. The free water of samples was measured by weight loss on drying powdered samples for 3 hr. at 100°C.

It was known by preliminary tests that when the sample containing much water was powdered finely and recorded by X-ray a remarkable change took place in the sample during this procedure. In order to determine the mineral content of samples without the change during analytical procedure the samples were washed with pure ethyl alcohol, filtered, dried at room temperature in vacuum desiccator in several minutes and tested by X-ray diffractometer. In this case the free water of samples was eliminated and the salts dissolved in the water were crystallized. The mineral content of the original sample was calculated multiplying the value of X-ray analysis by (100-free water %)/100. The results are shown in Fig. 7.

Figure 7 illustrates that the following chemical reactions take place partly soon after the mixing of raw materials and extensively by the addition of ammonia and water.

$$Ca(H_2PO_4)_2 \cdot H_2O + (NH_4)_2SO_4 = 2NH_4H_2PO_4 + CaSO_4 + H_2O \quad \text{.....(1)}$$

$$(NH_4)_2SO_4 + CaSO_4 + H_2O + (NH_4)_2SO_4 \cdot CaSO_4 \cdot H_2O \quad \text{.....(2)}$$

$$CaSO_4 \cdot 1/2H_2O + (NH_4)_2SO_4 + 1/2H_2O = (NH_4)_2SO_4 \cdot CaSO_4 \cdot H_2O \quad \text{.....(3)}$$

$$H_3PO_4 + NH_4OH = NH_4H_2PO_4 + H_2O \quad \text{.....(4)}$$

$$2KCl + (NH_4)_2SO_4 = K_2SO_4 + 2NH_4Cl \quad \text{.....(5)}$$

$$K_2SO_4 + Ca(H_2PO_4)_2 \cdot H_2O = 2KH_2PO_4 + CaSO_4 + H_2O \quad \text{.....(6)}$$

$$K_2SO_4 + CaSO_4 + H_2O = K_2SO_4 \cdot CaSO_4 \cdot H_2O \quad (7)$$

$$mKH_2PO_4 + nNH_4H_2PO_4 \rightarrow \text{crystalline solution} \quad \text{.....(8)}$$

$$r[(NH_4)_2SO_4 \cdot CaSO_4 \cdot H_2O] + s(K_2SO_4 \cdot CaSO_4 \cdot H_2O) \rightarrow \text{crystalline solution} \quad \text{.....(9)}$$

$$2KH_2PO_4 + (NH_4)_2SO_4 \cdot CaSO_4 \cdot H_2O = 2NH_4H_2PO_4 + K_2SO_4 \cdot CaSO_4 \cdot H_2O \quad (10)$$

Potassium sulfate formed by reaction 5 reacts

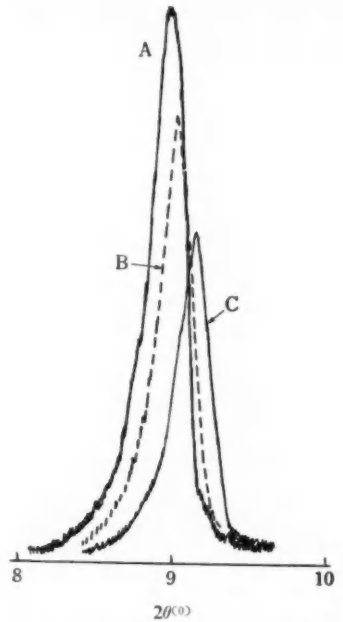


Fig. 5. Change of diffraction peak of crystalline solution of syngenite.
Weight ratios of ammonium and potassium syngenite are: A 66 : 34; B 50 : 50; C 24 : 76.

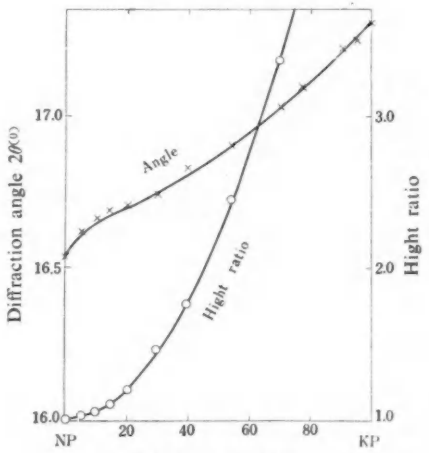


Fig. 6. Relation between weight ratio of monoammonium phosphate (NP) component and monopotassium phosphate (KP) component in their crystalline solution and diffraction angle of center of the peak and also the ratio of height of the peak of NP and that of the crystalline solution.

immediately to form potassium syngenite (7) and monopotassium phosphate(6) and does not actually exist in samples. Reactions 1-9 were almost completed when the granules were dried for 15 min. in a 130°C oven. At this time the free water of the sample was 8.52%.

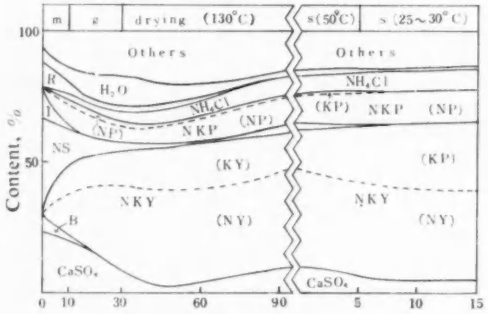


Fig. 7. Change of mineral content of samples in the midst of production process.
m=mixing, g=granulation, s=storing in sealed bottles, R=KCl, I=$Ca(H_2PO_4)_2 \cdot H_2O$, NP=$NH_4H_2PO_4$, KP=$KH_2PO_4$, NKP=crystalline solution of NP and KP, NS=$(NH_4)_2SO_4$, KY=$K_2SO_4 \cdot CaSO_4 \cdot H_2O$, NY=$(NH_4)_2SO_4 \cdot CaSO_4 \cdot H_2O$, NKY=crystalline solution of NY and KY, B=$CaSO_4 \cdot 1/2H_2O$.

It was clarified that by further drying a part of syngenite was decomposed to form calcium sulfate anhydride and ammonium sulfate. When dried for 60 min. the free water of the sample was 2.91% and the content of ammonium sulfate and calcium sulfate anhydride increased to a fair extent (Fig. 7). After being stored for days in a sealed bottle at 50°C the free water and those minerals decreased to form syngenite and the grains of the sample slightly adhered to each other forming a cake. When the granulated sample was dried at 120°C for 60 min. the free water content of the sample was 4.32%. Decomposition of syngenite took place similarly. After being stored for days at 50°C the grains adhered to each other more firmly than they did in the above sample.

The reaction 10 took place gradually and continued even in storing at room temperature. By this reaction $NH_4/K$ ratio of crystalline solution of syngenite decreased and that of monophosphate increased.

Samples of 8-8-5 mixed fertilizer in the midst of each process of large scale production were tested in the same way. It was clarified that the above reactions took place similarly but often more slowly than in the laboratory test, perhaps because the raw materials were not mixed so well as in the laboratory. A greater amount of calcium sulfate anhydride and ammonium sulfate and less syngenite were contained in the sample before piling. The sample after being piled and caked contained a very small amount of free water and these salts.

**Thermal Decomposition of Syngenite.**—Figure 8 illustrates the weight loss of synthetic ammonium and potassium syngenite and crystalline solution of equal weight of the two when heated at a rate of 3~4°C/min. Ammonium syngenite was decomposed over 110°C. Over 160°C ammonium sulfate was volatilized. 1 : 1 syngenite or potassium syngenite was decomposed over 120°C or 240°C respectively. The syngenite contained in commercial fertilizer 8-8-6 or 8-8-5 resembled 1 : 1 syngenite and was not decomposed by heating for hours at 120°C. Ammonium syngenite was not decomposed by heating for hours at 100°C. However, it was clarified that the syngenite just after its formation in mixed fertilizer e. g. just after the granulation or at the begining of drying was partly decomposed

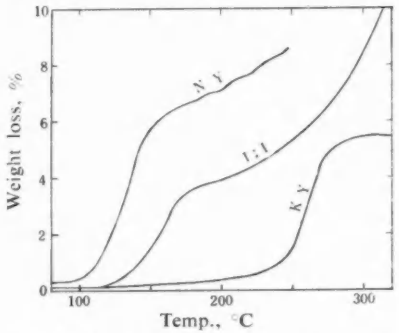


Fig. 8. Thermal decomposition of syngenite.
NY=ammonium syngenite, KY=potassium syngenite, 1 : 1=crystalline solution of the two 1 : 1 by weight.

even by heating at 100°C, perhaps because syngenite crystals had not grown well and a small amount of impurities such as $HPO_4^{2-}$ instead of $SO_4^{2-}$ was contained in the crystal.

To determine exactly the free water content of such samples by heating at 100°C, the amount of crystallization water lost by the heating must also be measured determining the amount of syngenite decomposed.

## Discussion

It seems that syngenite, especially ammonium-rich syngenite plays an important role concerning the caking of products in a storage pile. In the preparation of standard samples it was observed that potassium rich syngenite was formed quickly and had little tendency of hardening and that ammonium-rich syngenite was formed slowly and hardened. Moreover, ammonium-rich syngenite is apt to decompose on drying and recrystallize during piling.

It has been known that mixed fertilizers such as 8-7-8, 8-8-6 and 8-8-5 are apt to form a hard cake and that the fertilizers such as 3-10-10, 3-10.5-5 etc. have little tendency of caking in a storage pile. This is attributable to the fact that the latter contain less and the former much ammonium syngenite component.

In large scale plants the granules are often dried in shorter time at a higher temperature than was done in the laboratory experiment. Thermal decomposition of syngenite must take place remarkably on the surface of grains which are dried enough and reach a high temperature. Free water remains in the inner part of the grains and gradually disperses to the surface to cause the recrystallization of syngenite and the caking of products. By the crystallization of syngenite the free water content of the products is reduced and a part of the salts dissolved in the water is crystallized promoting the formation of a hard cake.

The reaction 10 takes place successively in a storage pile. When the raw materials were not powdered finely or mixed well, reactions 1–9 are not completed before piling but occur continuously in the storage pile. All of these reactions are promoted by free water in the granules.

In order to prevent the caking of products (1) free water of the granules must be reduced as far as possible by drying, (2) drying at high temperature must be avoided so as to depress the thermal decomposition of syngenite, (3) the raw materials had better be powdered and mixed well so that the reactions 1–9 are almost finished before piling, and (4) the dried sample had better be cooled to a lower temperature. Of course it is desirable not to pile the products too high.

It was observed that ammonium chloride was volatilized slightly by heating at 130°C. In the drier of the large scale plant a small amount of ammonium chloride must be volatilized. Also for this reason the granules must not be dried at a high temperature.

Measurement of the amount of free and crystallization water of the products is nesessary for calculation of material balance. It was clarified that water of crystallization was contained only in syngenite and that its amount could be measured by X-ray determination of syngenite. The free water content of products stored for more than a week after granulation could be measured almost exactly by drying the samples for 3 hr. at 100°C. To measure the free water content of samples soon after production by the above method the loss of crystallization water by the drying must also be measured, determining the amount of syngenite before and after the drying. By such a method the material balance of mixed fertilizer could be calculated exactly.

## Summary

The mineral content of mixed fertilizer produced with calcium superphosphate, ammonium sulfate and potassium chloride and also the reactions during the production process were investigated by X-ray diffraction.

It was observed that remarkable reactions took place between monocalcium phosphate, calcium sulfate, ammonium sulfate and potassium chloride by the addition of water for granulation. At the beginning of drying of the wet granules these minerals almost disappeared to form ammonium chloride and crystalline solutions of ammonium and potassium syngenite and those of monoammonium and monopotassium phosphate.

The syngenite thus formed decomposed partly by further drying and again formed while the product was placed in a storage pile. It seems that the caking of the product which often occurs in a storage pile is caused mainly by the crystallization of syngenite which decreases the amount of free water in the product and makes other salts crystallize at the same time.

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# *An Empirical Method for Estimating Normal Boiling Point and other Physical Properties of Alkene Hydrocarbons*

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The structural variation in the physical properties of alkene hydrocarbons is determined by the number and relative position of double bonds and side chains in the molecule. Owing to the presence and mutual influence of two different kinds of chemical bonds and side chains, correlation between properties and molecular structure is far more complicated than that in the case of isoparaffins, for which an elaborate set of structural parameters can be successfully used[1,2]. Although a few attempts were made to correlate the boiling point[3,4] or critical constants[5,6] with the molecular structure of alkenes, no extensive method has been established at the present stage.

In this paper, an empirical relation between the physical properties of linear and branched alkenes and their molecular structure is proposed. The "effective carbon number" method which has been used for isoparaffins in the previous report[2] is again adopted. As will be shown later, a characteristic constant called "effective carbon number" can be defined for all the alkene hydrocarbons. Thus, this effective carbon number is first calculated by the proposed equation and then, by the use of a previously presented nomogram[2], the normal boiling point and other physical properties of the alkenes can be estimated from the knowledge of the structural formula alone.

## Effective Carbon Number

When the boiling points of normal paraffins are plotted against the number of carbon atoms, a family of curves for different pressures is obtained. Then, reading the boiling points of a given alkene on these curves, one can obtain a set of values of an "effective number" of carbon atoms, each corresponding to every different pressure. These sets of values for several alkenes obtained by this procedure are listed in Table I together with the used values of the boiling point[7,8], where a reasonable constancy of the values is observed over a considerably wide range of pressure. This effective number of carbon atoms depending on the structural feature of each compound but not on the external condition is called the "effective carbon number" and hereafter denoted by $n^*$. It is shown that the proper assignment of the $n^*$ value is advantageous not only for the estimation of the boiling point of the alkenes at various external pressures but also for that of other physical properties such as the critical constants, as in the case of isoparaffins[2].

TABLE I. CONSTANCY OF EFFECTIVE CARBON NUMBER OF ALKENES AT VARIOUS EXTERNAL PRESSURES

| Compound | Pressure, mmHg | 10 | 20 | 60 | 200 | 400 | 760 |
|---|---|---|---|---|---|---|---|
| 1-Butene | $T_b$[7] (°C) | −81.5 | −72.89 | −57.15 | −36.10 | −21.62 | −6.26 |
| | $n^*$ | 3.88 | 3.87 | 3.86 | 3.86 | 3.86 | 3.85 |
| 2-Methylpropene | $T_b$[7] (°C) | −81.95 | −73.37 | −57.664 | −36.666 | −22.227 | −6.900 |
| | $n^*$ | 3.87 | 3.85 | 3.84 | 3.85 | 3.84 | 3.84 |
| 1,3-Butadiene | $T_b$[8] (°C) | −79.7 | −71.0 | −55.1 | −33.9 | −19.3 | −4.5 |
| | $n^*$ | 3.92 | 3.93 | 3.93 | 3.90 | 3.89 | 3.86 |

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### Structural Units

The molecular structure of alkenes can be specified by the number and the relative position of double bonds and those of branching units. Therefore, if the mutual influence among these units is properly estimated, the deviation of the effective carbon number from the real one may be expressed as a linear combination of several factors, each corresponding to a double bond or a branching unit. Although various kinds of methods for such factorization would be possible, only the linear factorization is used here because of its simplicity for practical purposes.

The following four groups of carbon atoms are adopted as the structural units of alkenes: i. e. (I) double bond existing in the linear portion of the molecule, (II) double bond attached to branching atoms, (III) trifunctional branching and (IV) tetrafunctional branching. Schematically, these are

(I) $-C=C-$, (II) $-C=\overset{|}{\underset{|}{C}}-C-$ or $-C-\overset{|}{\underset{|}{C}}=\overset{|}{\underset{|}{C}}-C-$,

(III) $-C-\overset{|}{\underset{|}{C}}-C-$ and (IV) $-C-\overset{|}{\underset{|}{\overset{|}{\underset{|}{C}}}}-C-$

For each of the four structural units, the following equation is obtained after some troublesome analysis of available boiling point data:

$$\Delta n_{\mathrm{I}} = 0.24 - 0.12b_1 + 0.05b_2 \quad (1)$$

$$\Delta n_{\mathrm{II}} = 0.24 - 0.08b_1 + 0.07b_2 \quad (2)$$

$$\Delta n_{\mathrm{III}} = 0.28 - 0.06c_2 + 0.06c_3 \quad (3)$$

$$\Delta n_{\mathrm{IV}} = 0.73 - 0.14c_2 + 0.05c_3 \quad (4)$$

The difference of the effective carbon number $n^*$ from the real carbon number $n$ is then given by the sum of these contributions,

$$\Delta n = n - n^* = \sum_{\mathrm{I}} \Delta n_{\mathrm{I}} + \sum_{\mathrm{II}} \Delta n_{\mathrm{II}} + \sum_{\mathrm{III}} \Delta n_{\mathrm{III}} + \sum_{\mathrm{IV}} \Delta n_{\mathrm{IV}} \quad (5)$$

where the summation extends over all structural units of each type. The four parameters, $b_1$, $b_2$, $c_2$ and $c_3$, in Eqs. 1 to 4 are defined as follows:

- $b_1$—the number of carbon-carbon bonds adjacent to the double bond.
- $b_2$—the number of carbon-carbon bonds (single and double) next but one to the double bond.
- $c_2$—the number of the second neighbor carbon atoms of the branching point (tertiary or quaternary carbon atom).
- $c_3$—the number of the third neighbor carbon atoms of the branching point (tertiary or quaternary carbon atom).

As is easily seen, the intrinsic contribution of the structural unit I, III and IV is represented by the first term of Eqs. 1, 3 and 4, respectively, while two other terms which represent the contribution of adjacent carbon atoms to each structural unit are introduced to take the mutual correlation of the structural units into account. The choice of type II as an independent structural unit is also due to the fact that the correlation of the double bond with the branching is so strong that it can not be treated separately.

It is obvious from the definition that the effective carbon number of isoparaffins is given by

$$n^* = n - \sum_{\mathrm{III}} (0.28 - 0.06c_2 + 0.06c_3) - \sum_{\mathrm{IV}} (0.73 - 0.14c_2 + 0.05c_3) \quad (6)$$

The accuracy of this equation is of the same degree as that of Eq. 41 in the previous paper[2], which is expressed in terms of the Wiener parameters[1].

### Example of Calculation

The present method consists of the following two procedures:

(1) Effective carbon number $n^*$ is calculated by Eq. 5. Only the structural formula of alkene in question is required.

(2) The vapor pressure-temperature relationship, the critical constants and the heat of vaporization at normal boiling point can be read on nomogram[2] by using the value of $n^*$ just obtained.

For clear understanding of the method, calculation of the normal boiling point of 3, 5, 5-trimethyl-1-hexene is presented as an example.

3, 5, 5-Trimethyl-1-hexene

$$C^1=C^2-C^3(-C^7)-C^4-C^5(-C^8)(-C^9)-C^6$$

This compound contains the aforementioned structural units of I, III and IV types. The unit of type I is attached to one carbon-carbon bond to be counted as $b_1$, say $C^2$-$C^3$, and to two bonds to be counted as $b_2$, say $C^3$-$C^4$ and $C^3$-$C^7$; hence

$$\Delta n_{\mathrm{I}} = 0.24 - 0.12 \times 1 + 0.05 \times 2 = 0.22$$

The structural unit of type III or tertiary carbon atom $C^3$ has two second neighbors, say $C^1$ and $C^5$, and three third neighbors, say $C^6$, $C^8$ and $C^9$, hence

$$\Delta n_{\mathrm{III}} = 0.28 - 0.06 \times 2 + 0.06 \times 3 = 0.34$$

Quaternary carbon atom $C^5$ has one second neighbor, $C^3$, and two third neighbors, $C^2$ and $C^7$, and so

$$\Delta n_{\mathrm{IV}} = 0.73 - 0.14 \times 1 + 0.05 \times 2 = 0.69$$

TABLE II. NORMAL BOILING POINT OF MONOALKENES

| Compound | Normal boiling point $T^{\circ}_b$, °C | | Effective carbon number, $n^*$ | |
|---|---|---|---|---|
| | Obs.[9] | Calcd. | Obs. | Calcd. |
| Ethylene | −103.7 | −104.0 | 1.76 | 1.76 |
| Propylene | −47.7 | −47.0 | 2.86 | 2.88 |
| 1-Butene | −6.3 | −6.0 | 3.85 | 3.83 |
| 2-Butene | 1. | 2.0 | 4.04 | 4.00 |
| 2-Methylpropene | −6.9 | −2.0 | 3.84 | 3.92 |
| 1-Pentene | 29.9 | 30.0 | 4.83 | 4.83 |
| 2-Pentene | 36.1 | 34.0 | 5.00 | 4.95 |
| 2-Methyl-2-butene | 38.6 | 36.0 | 5.07 | 5.00 |
| 2-Methyl-1-butene | 31.2 | 31.0 | 4.86 | 4.85 |
| 3-Methyl-1-butene | 20.1 | 20.0 | 4.55 | 4.56 |
| 1-Hexene | 63.5 | 63.0 | 5.83 | 5.83 |
| 2-Hexene | 68.2 | 67.0 | 5.98 | 5.95 |
| 3-Hexene(*trans*) | 67.1 | 65.0 | 5.93 | 5.90 |
| 2-Methyl-1-pentene | 62.2 | 63.0 | 5.80 | 5.85 |
| 3-Methyl-1-pentene | 54.2 | 56.0 | 5.54 | 5.62 |
| 4-Methyl-1-pentene | 53.9 | 54.0 | 5.53 | 5.55 |
| 2-Methyl-2-pentene | 65.0 | 66.0 | 5.88 | 5.93 |
| 3-Methyl-2-pentene | 68.0 | 66.0 | 5.97 | 5.93 |
| 4-Methyl-2-pentene | 57.0 | 56.0 | 5.60 | 5.62 |
| 2-Ethyl-1-butene | 64.7 | 62.0 | 5.76 | 5.78 |
| 2,3-Dimethyl-1-butene | 55.6 | 51.0 | 5.58 | 5.46 |
| 3,3-Dimethyl-1-butene | 41.2 | 41.0 | 5.14 | 5.14 |
| 2,3-Dimethyl-2-butene | 73. | 71.0 | 6.1 | 6.08 |
| 1-Heptene | 93.6 | 93.0 | 6.83 | 6.83 |
| 2-Heptene | 98.5 | 97.0 | 7.00 | 6.95 |
| 3-Heptene | 95.6 | 95.0 | 6.90 | 6.90 |
| 2,3,3-Trimethyl-1-butene | 77.9 | 77.0 | 6.30 | 6.26 |
| 1-Octene | 121.3 | 120.0 | 7.83 | 7.83 |
| 2-Isopropyl-3-methyl-1-butene | 113.6 | 100.0 | 7.55 | 7.08 |
| 1-Nonene | 146.9 | 147.0 | 8.84 | 8.83 |
| 2,3,3,4-Tetramethyl-1-pentene | 133.2 | 133.0 | 8.30 | 8.32 |
| 1-Decene | 170.6 | 170.0 | 9.84 | 9.83 |
| 2,3,3,4,4-Pentamethyl-1-pentene | 158.8 | 157.0 | 9.33 | 9.27 |

$n^*_{obs}$ = Effective carbon number at normal boiling point (cf. Table I)
$n^*_{calcd}$ = Calculated value by Eq. 5

Thus, the summing up of the above three $\Delta n_j$'s gives,

$$\Delta n = 0.22 + 0.34 + 0.69 = 1.25$$

$$\text{or} \quad n^* = 9 - 1.25 = 7.75$$

Then, using the nomogram[2], 118°C is obtained for the normal boiling point which is to be compared with the observed value 119.4°C[9].

### Comparison with Experimental Data

A test of the present method by the procedure described in the last section was carried out for 188 monoalkenes and 46 dialkenes.

The average deviation of the calculated values of normal boiling point of the monoalkenes from the literature values[9,10] was as small as 2.5°C, with the maximum deviation −17°C for 2-*tert*-butyl-3,3-dimethyl-1-butene. Only ten percent of the tested compounds showed an error higher than 5°C. Table II shows about 30 examples of this test.

In the case of dialkenes with no "conjugated double bond", the average deviation of the normal boiling point was found to be about 2.4°C, the maximum deviation was −11°C for 1,4-heptadiene, and the deviation was less than 5°C for 87 percent of the tested compounds. Table III shows the results for typical examples.

In the presence of the conjugated double

9) G. Egloff, "Physical Constants of Hydrocarbons" Vol. V, Reinhold Publishing Corporation, New York, (1953).

10) S. W. Ferris, "Handbook of Hydrocarbons", Academic Press Inc., New York (1955).

TABLE III. NORMAL BOILING POINT OF DIALKENES

| Compound | Normal boiling point $T^0_b$, °C | | Effective carbon number, $n^*$ | |
|---|---|---|---|---|
| | Obs.[10] | Calcd. | Obs. | Calcd. |
| 1,4-Hexadiene | 65. | 61.0 | 5.88 | 5.78 |
| 1,5-Hexadiene | 59.5 | 58.0 | 5.70 | 5.66 |
| 2-Methyl-1,4-pentadiene | 56. | 59.0 | 5.60 | 5.70 |
| 3-Methyl-1,4-pentadiene | 55. | 49.0 | 5.57 | 5.40 |
| 1,4-Heptadiene | 100.8 | 90.0 | 7.10 | 6.73 |
| 1,5-Heptadiene | 94.3 | 91.0 | 6.85 | 6.78 |
| 2-Methyl-1,5-hexadiene | 92.1 | 89.0 | 6.78 | 6.68 |
| 3-Methyl-1,5-hexadiene | 80.5 | 82.0 | 6.39 | 6.46 |
| 5-Methyl-1,4-hexadiene | 91.8 | 91.0 | 6.77 | 6.76 |
| 2,4-Dimethyl-1,4-pentadiene | 81.3 | 89.0 | 6.41 | 6.70 |
| 1,7-Octadiene | 117.5 | 116.0 | 7.69 | 7.66 |
| 3-Methyl-1,5-heptadiene | 110.5 | 112.0 | 7.44 | 7.51 |
| 2-Methyl-1,6-heptadiene | 115.6 | 116.0 | 7.65 | 7.68 |
| 2,4-Dimethyl-1,5-heptadiene | 132.1 | 134.0 | 8.29 | 8.41 |
| 2,6-Dimethyl-2,6-octadiene | 166.9 | 169.0 | 9.67 | 9.86 |

$n^*_{obs}$ = Effective carbon number at normal boiling point (cf. Table I)
$n^*_{calcd}$ = Calculated value by Eq. 5

TABLE IV. COMPARISON OF CALCULATED CRITICAL CONSTANTS AND HEAT OF VAPORIZATION WITH LITERATURE VALUES

| Compound | Effective carbon number, $n^*$ | Critical temperature °K | | | Critical pressure atm. | | | Heat of vaporization (kcal./mol.) at $T^0_b$ | | at 25°C | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | Calcd. | Obs.[7] | Calcd. | Thodos[5] | Obs.[7] | Calcd. | Thodos[5] | Obs.[7] | Calcd. | Obs.[7] | Calcd. |
| Ethylene | 1.76 | 282.4 | — | 290.3 | 50.0 | — | 50.7 | 3.24 | — | — | — |
| Propylene | 2.88 | 365.0 | 363.0 | 367.3 | 45.6 | 43.0 | 45.7 | 4.40 | 4.36 | — | 3.27 |
| 1-Butene | 3.83 | 419.6 | 415.0 | 425.3 | 39.7 | 37.0 | 39.8 | 5.24 | 5.14 | 4.87 | 4.70 |
| 2-Butene (*cis*) | 4.00 | 430.2 | 424.0 | 429.3 | 41. | 38.0 | 37.4 | 5.58 | 5.27 | 5.30 | 4.95 |
| (*trans*) | | | | 426.3 | | | 37.3 | 5.44 | | 5.15 | |
| 2-Methylpropene | 3.92 | 417.9 | 422.0 | 425.2 | 39.5 | 36.0 | 40.4 | 5.29 | 5.22 | 4.92 | 4.84 |
| 1-Pentene | 4.83 | 474.2 | 461.0 | 471.4 | 40. | 34.0 | 35.2 | — | 5.95 | — | 6.02 |
| 2-Pentene | 4.95 | 475.6 | 466.0 | 471.5 | 40.4 | 34.0 | 32.9 | — | 6.05 | — | 6.19 |
| 2-Methyl-2-butene | 5.00 | 470.2 | 468.0 | 471.2 | 34. | 33.0 | 33.2 | — | 6.09 | — | 6.06 |
| 2-Methyl-1-butene | 4.85 | — | 462.0 | 471.6 | — | 34.0 | 35.6 | — | 5.97 | — | 6.25 |
| 3-Methyl-1-butene | 4.56 | 464.8 | 450.0 | — | 33.9 | 35.0 | — | — | 5.75 | — | 5.69 |

bond, Eq. 5 fails to express the difference of the effective carbon number of compounds from the real carbon number. However, the effective carbon number itself can also be defined for this type of compound (see Table I), and a conventional procedure is possible. That is, if one boiling point datum is available, $n^*$ can be obtained on nomogram without the aid of Eq. 5.

Table IV shows the comparison of the estimated values of critical temperature, critical pressure and heat of vaporization with the observed values[7], where the critical constants estimated by the Thodos' method[5,6] are also given for comparison.

The application of Eq. 6 to isoparaffins is also satisfactory, though the results are not given here*3. It is especially favorable for the estimation of the heat of vaporization at normal boiling point and the critical temperature.

## Summary

A method of estimating the structural variation in the boiling point and other physical properties of alkenes is developed. By this method, all properties are expressed in terms of a structural constant called the "effective carbon number" which depends on the number and relative position of double bonds and those of side chains but not on external variables such as the temperature. An empirical equation is presented to correlate the effective carbon number with molecular structure. By combining the use with the previously presented nomogram*4, it is proved to be quite

*3 Details of the results will be published elsewhere.

*4 Copies of original drawing of the nomogram will be sent upon request.

useful for rapid evaluation of various properties including the temperature-vapor pressure relationship and the critical constants.

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# *Studies on Organophosphorus Compounds. I. The Reaction of O,O-Dimethyl Phosphonate with p-Benzoquinone*

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It is well known that phosphonates* having phosphorus-hydrogen linkage react with the carbonyl groups as aldol-condensation to produce $\alpha$-hydroxy phosphonate[1]:

$$C_6H_5CHO + HP(O)(OH)_2 \rightarrow C_6H_5CH(OH)P(O)(OH)_2$$

Ville[2] and Marie[3] studied this reaction with various ketones and aldehydes from 1889 to 1904.

Recently, it has been well known that Dipterex[4] was prepared by this reaction of *O,O*-dimethyl phosphonate with chloral, which proved to be very useful as an insecticide.

$$(CH_3O)_2P(O)H + OHC\cdot CCl_3 \rightarrow (CH_3O)_2P(O)\overset{OH}{\overset{|}{C}}HCCl_3$$

Furthermore, Sallman et al.[5] have reported that *O,O*-dialkyl phosphonates react with $\alpha,\alpha'$-dihalo-ketones to produce $\alpha$-hydroxy-$\beta,\beta'$-dihalo phosphonates which are also useful as an insecticide.

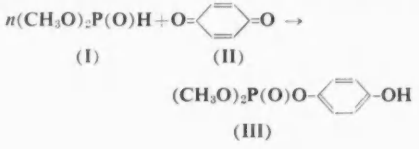
The products of this reaction, $\alpha$-hydroxy-$\beta$-halo phosphonates, have not only the agricultural usefulness but also a very interesting property which is that the phosphonates are changed to vinyl phosphorates under the presence of alkaline[6-8].

$$(CH_3O)_2P(O)\overset{OH}{\overset{|}{C}}H\cdot CCl_3 \xrightarrow{NaOH} (CH_3O)_2P(O)CCH{=}CCl_2$$

Thus, the reaction of phosphonate having the phosphorus-hydrogen linkage with carbonyl groups of aldehydes or ketones were studied widely, but the reaction with the carbonyl group of benzoquinone has not been reported yet.

During the course of an investigation of organophosphorus compounds, the present author found that the reaction of *O,O*-dimethyl phosphonate with carbonyl group of *p*-benzoquinone did not produce the usual $\alpha$-hydroxy phosphonate but the phosphorate having *p*-hydroxy-phenyl group.

The reaction of two moles ratio of *O,O*-dimethyl phosphonate with one mole ratio of *p*-benzoquinone produced undistillable pale yellow oil. This product was purified by acetone and ligroin. The refractive index and the infrared absorption spectrum of this product was not changed by the purification using silica-gel column-chromatography. So, it was considered that this product was a pure substance. The microanalytical data of this product showed that this product was composed of one mole ratio of *O,O*-dimethyl phosphonate and one mole ratio of *p*-benzoquinone. Moreover, the reaction product of one mole ratio of *O,O*-dimethyl phosphonate and one mole ratio of *p*-benzoquinone showed the same refractive index, infrared absorption spectrum and microanalytical data as the above product.




* Phosphorus compounds in this paper were named according to the Drake Comittee's Report (*Chem. Eng. News*, **30**, 4515 (1952)).

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2) J. Ville, *Compt. rend.*, **107**, 659 (1888); **109**, 71 (1890); **110**, 384 (1890).
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4) W. Lovenz, U. S. Pat. 2701225.
5) R. Sallman, D. R. Pat. 1000364.
6) W. F. Barthel, *J. Am. Chem. Soc.*, **77**, 2424 (1955).
7) W. Lorenz, ibid., **77**, 2554 (1955).
8) W. Perkow, D. R. Pat. 1024945.